Clinical Orthopaedics

ANTHONY F. DePALMA
Editor-in-Chief

Number Nine

Spring, 1957

J. B. LIPPINCOTT COMPANY
Philadelphia and Montreal

Distributed in Great Britain by Pitman Medical Publishing Co., Limited, London

Library of Congress Catalog Card Number 53-7647

Clinical Orthopaedics is designed for the publication of original articles offering significant contributions to the advancement of surgical knowledge.

Original, typed manuscripts, not carbon copies, *and illustrations should be forwarded prepaid to* Dr. Anthony F. DePalma, 1025 Walnut Street, Philadelphia 7, Pa.

Manuscripts should be typed double spaced on one side of standard typewriter paper, leaving wide margins. While every effort will be made to guard against loss, it is advised that authors retain copies of manuscripts submitted. All pages should be numbered. Dorland's *American Illustrated Medical Dictionary* (edition 22) and Webster's *New International Dictionary* (edition 2) should be used as standard references. Scientific names for drugs should be used when possible. Copyright or trade names of drugs should be capitalized. Units of measurement, e.g., dosage, should be expressed in the metric system. Temperature should be expressed in degrees centigrade. A contribution in a foreign language, when accepted, will be translated and published in English.

Black-and-white illustrations will be reproduced free of charge, but the publisher reserves the right to establish a reasonable limit upon the number. Ordinarily, colored illustrations cannot be published except at the author's expense. Black-and-white photographs should be in the form of glossy prints These should not be defaced in any way. Any changes desired in them should be marked on a tissue overlay. This should be done before it is pasted to the print, since it is important not to mar the print in any way. Or any changes may be indicated on a separate sheet of paper Line and wash drawings should be on white art board, with lettering in black India ink large enough to be readable after [illegible]

[illegible] tions of the same to facilitate their circulation among *the members of the editorial board. Illustrations* should be numbered, the tops indicated, and the author's name and the title of the article in brief should appear on the back. However, this should be done lightly, so as to leave no imprint on the *face of the illustration. A separate typewritten* sheet of legends for the illustrations should be supplied.

A bibliography of numbered references *in alphabetic order* should appear at the end of the manuscript *with corresponding numbering in the text.* Bibliographies should conform to the style of the *Quarterly Cumulative Index Medicus.*

If a book:

Author's name, title of book, edition if there is more than one, page numbers if it is wished to direct the reader to a specific section of the book, publisher's name, city, year of publication of book, in the order named.

If an article in a journal:

Author's name, title of article, volume number, inclusive page numbers, year of publication, in the order named.

Manuscript may be submitted to us in the original language of the author. Now it is our policy to handle the translation of these articles by our office without cost to the contributor if the article is found to be acceptable for publication.

[illegible] lingua.

Following are the general subjects of forthcoming issues of *Clinical Orthopaedics*·

Affections of Growth Centers (Epiphyses, Apophyses), Fall, 1957
Orthopaedic Surgery in the Geriatric Patient, Spring, 1958
Rehabilitation, Fall, 1958
The Hand, Part 1, *Spring, 1959*
The Hand, Part 2, Fall, 1959

All contributors desiring to submit articles for consideration for publication on the topics listed above *or in the general sections of this publication should submit them to* the editor some months in advance of the date of the issue for which they are intended

PRINTED IN THE UNITED STATES OF AMERICA

Contents

SECTION II
GENERAL ORTHOPAEDICS

SECTION III

Motorist Injuries and Motorist Safety

PRIMARY MOTORIST SAFETY: PREVENTION OF ACCIDENTS

(Part 3)

GUEST EDITOR: JACOB KULOWSKI, M.D.
Saint Joseph, Missouri



John Albert Key

chondria to zymogen granules," written in 1916, to his last work with Conwell, *The Management of Fractures, Dislocations and Sprains,* in its sixth edition at the time of his death, one finds erudite and valuable writing on every phase of the study of orthopaedics, with occasional sorties into other fields.

The delicate perfection of the organization of his time permitted him to attend with regularity the meetings of the many scientific societies of which he was a member. It has been said that "he never missed a meeting of the American Orthopaedic Association," and he was President of that august body during 1945 and 1946. Yet his social life was not neglected. Indeed, his presence at any social function was a signal for its immediate success His interests were so broad that never was he known to be at a loss for an appropriate topic with which to command the attention of any group. Sports (he was an inveterate fisherman), social and economic problems, various phases of scientific endeavor—he could speak interestingly about them all. Further, he could lead conversation into pertinent discussion with ease, thus offering everyone who participated a chance to express himself and, if the discussion persisted, add his own valuable and constructive criticism.

Among the many scientific societies of which he was a member were the American Medical Association, the American Surgical Association, the American College of Surgeons, the American Academy of Orthopaedic Surgeons, the American Radium Society, the Missouri Medical Association, the Orthopaedic Research Society, the Southern Medical Association, the Southern Surgical Association and the Robert Jones Club. On a certain occasion at a meeting of this club he had been assigned the task of organizing the program for a future meeting. His co-workers were so co-operative that he was hard pressed to choose his speakers. Everyone had volunteered! But, with his usual graciousness and tact he made his choice in such a manner that no one felt slighted. And, when the meeting had ended, he invited the entire membership of the Club home to dinner.

As might be expected in a man of so many talents, Dr. Key was a dynamic speaker. I have read and reread his presidential address to the American Orthopaedic Association, "Education and Certification of Orthopaedic Surgeons." I believe that for those who intend to follow orthopaedic surgery it should be "required reading," and for those who already have made their mark in the discipline it could be reread with profit.

Albert Key was my friend, and his death to me is an immeasurable loss. Yet I am only one of a legion of men, young and old, who have felt the impact of his personality and, when faced in the years to come by a problem that seems beyond solution, will miss the aid that he was always so ready to give.

Dr. Key's writing has inspired and informed many of us, and recourse to it will prove an invaluable asset to every young man who plans on becoming a sound orthopaedic surgeon.

2

The Structure of Bone Mineral

AARON S. POSNER, PH.D.*

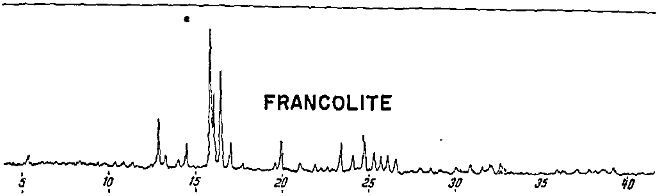


FIG. 1. X-ray diffraction pattern of powdered francolite (a carbonate-bearing fluorapatite mineral) taken on an x-ray spectrometer using geiger-counter detection of the copper K-α, Ni filtered, radiation. Abscissa in degrees; ordinate in arbitrary relative intensity units.

in the material and their spatial arrangement. By placing an x-ray detector (film, geiger counter, etc.) near the irradiated sample, it is possible to measure the angle between the incoming x-ray beam and the various outgoing diffracted beams. The detector also measures the relative intensities of the diffracted beams. Figure 1 illustrates an x-ray diffraction pattern of a sample of powdered francolite (a carbonate-bearing fluorapatite). In the figure the abscissa is the diffraction angle and the ordinate is the relative intensity of the diffracted beam. Each peak in the diagram represents a diffracted beam leaving the sample at a specific angle.

Another type of x-ray diffraction pattern is shown in Figure 2. This illustrates the result of passing a monochromatic x-ray beam through a single crystal of synthetic hydroxyapatite which was held in a definite crystal orientation. The powder sample used above (Fig. 1) was composed of many single crystals in random orientation. The x-ray pattern of a single crystal, here recorded on film as opposed to geiger-counter detection used in the powder work, consists of spots whose geometric arrangement and relative intensities are related to the crystal structure.

In an early study Mehmel[20] was able to calculate the arrangement of the constituent ions in the hydroxyapatite structure from x-ray diffraction data. Figure 3 shows the arrangement, according to Mehmel, of the ions in this mineral prototype of the inor-

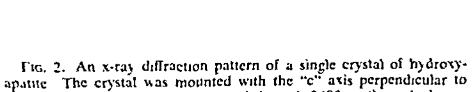


FIG. 2. An x-ray diffraction pattern of a single crystal of hydroxyapatite. The crystal was mounted with the "c" axis perpendicular to the incoming x-ray beam and rotated through 360° on this axis during the 4-hour exposure. The x-ray beam was copper K-α radiation unfiltered, and the detector was Kodak NO-SCREEN x-ray film.

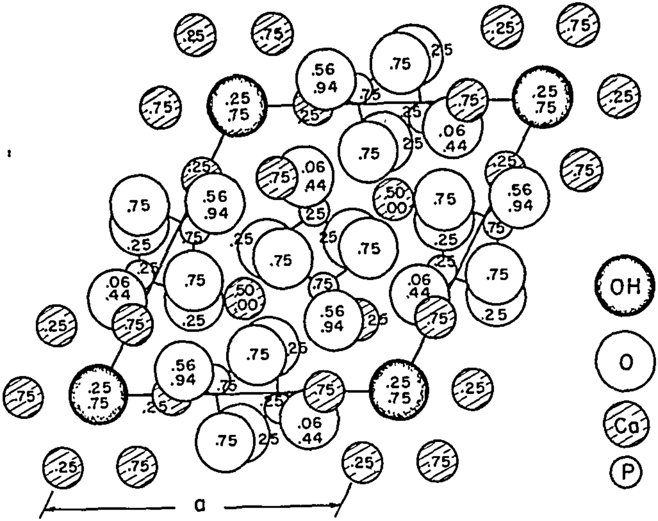


Fig. 3. The arrangement of the constituent atoms of hydroxyapatite, as reported by Mehmel,[20] shown in a projection on the basal plane. Modified from Carlström's drawing of fluorapatite.[4]

ganic portion of bone. The diagram shows that each phosphorus ion is surrounded by four equidistant oxygen ions, forming the orthophosphate (PO_4) group. The structure diagram also shows the spatial relationship between the calcium and hydroxyl ions and the orthophosphate groups.

The exact knowledge of the spatial arrangement of the constituents of a crystal is an aid in understanding the properties of the material. The following sections of this chapter will illustrate how crystallographic technics have shed light upon the nature of bone mineral. Further details on the theory and the technics of crystal chemistry, and in particular on x-ray diffraction, may be found in the textbooks of Bunn[3] and Klug and Alexander.[14]

BONE-CRYSTAL SIZE

As the crystal size of any material diminishes below about 0.1 micron in average diameter, the peaks or lines of the x-ray diffraction pattern begin to broaden. The broadening of a given peak is related to the crystal dimension in a direction in the crystal related to the diffraction angle. Thus, by measuring the x-ray line broadening, it is possible to calculate an average crystal dimension in a specific crystal direction.

In addition, a special technic known as low-angle x-ray scattering is used to study the broadening of the main beam (as opposed to the diffraction peaks) to estimate the fineness of the material. This method gives a particle size rather than a crystal

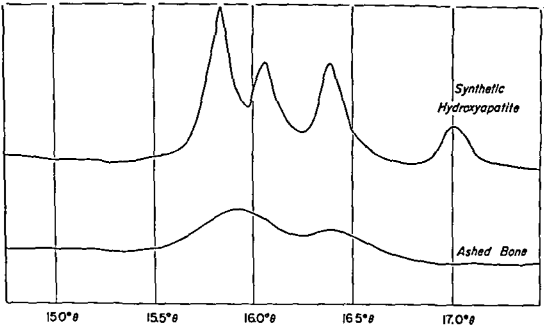


FIG. 4. Comparison of a portion of the x-ray diffraction patterns of powdered synthetic hydroxyapatite and thermally ashed rat bone. Line broadening due to small crystal size is apparent in the latter. Ordinate is in arbitrary relative intensity units; Ni filtered copper K-α radiation.



FIG 5 Electron micrograph of human cortical bone from tibia after autoclaving at steam pressure of 27 pounds for 4 hours. (R. A. Robinson and M. L. Watson)

dimension. In the study of bone mineral each submicroscopic particle appears to be a single crystal. Thus, in the case of bone the terms *crystal size* and *particle size* can be used interchangeably.

When bone mineral is studied by x-ray diffraction, the resulting pattern contains broadened, poorly resolved peaks. Figure 4 compares a portion of the x-ray diffraction pattern of powdered synthetic hydroxyapatite and thermally ashed rat bone. The lack of resolution of the major x-ray peaks is apparent in the latter when compared with the pattern from a well-crystallized material.

X-ray line broadening experiments[4,5] show that bone apatite crystals have an average growth in the "c" axis direction ranging from 155 A to 230 A. Low-angle scattering results[7,10] have suggested rod-shaped crystallites 220 A by 65 A, elongated in the "c" axis direction.

Extended electron-microscope studies by Robinson and Watson[36,37] have shown that bone crystals vary in size from below the resolving power of the instrument (about 25 A) to about 1,500 A, never growing large enough to be seen in the light microscope. These crystals are thin, tabular hexagons with the longest hexagonal axis parallel to the apatite "c" axis. These investigations never showed any of the rodlike bone crystals suggested by the low-angle x-ray scattering results. According to Robinson,[35] the crystal length and width are physiologically unimportant, since the tabular thickness remains in the range 25 to 75 A. Figure 5 shows an electron micrograph of a steam-autoclaved human bone, illustrating the work of Robinson and Watson in this field. Tabular bone crystals may be seen ranging from the threshold of resolution to about 1,500 A.

The crystal size derived from the above x-ray studies represent *average* diameters, while the electron microscope yields a survey of crystal sizes. The existence of a size distribution in bone crystals was corroborated in a recent x-ray study of steamed cow bone.[30] The method was based on a sug-

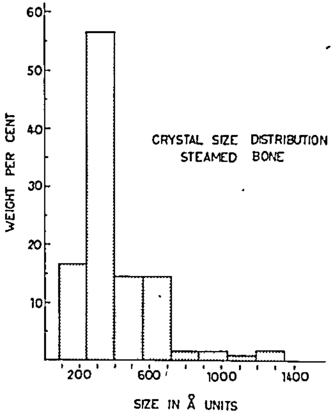


Fig. 6. Crystal-size distribution curve for a sample of steam-autoclaved cow bone. (Posner, A. S.: Thesis, Univ. of Liége, 1954)

gested extension of a Fourier analysis of the shape of a broadened reflection in the bone apatite x-ray pattern.[2,41] Figure 6 shows the results of this work. Note that at least 25 per cent of the bulk weight of the bone crystals have diameters larger than the average size. This curve is in excellent agreement with the distribution curve reported by Watson and Robinson[36] from electron micrographs.

Much information is needed on the subject of crystal size in bone mineral. Neuman and Neuman[26] ask whether or not bone apatite crystals vary in size and habit from species to species and whether or not crystals grow with age Add to this the need for data on the distribution of bone-crystal size and its biologic implications.

CRYSTAL STRUCTURE

General Considerations

Exclusive of the organic matrix, chemical analysis shows bone salt to contain Ca^{++},

PO_4^{---}, OH^-, carbon dioxide, citrate, water, Na^+, Mg^{++}, K^+, Cl^- and F^- and other components in trace amounts. As mentioned above, the x-ray diffraction pattern of bone salt resembles a poorly resolved hydroxyapatite pattern. Attempts to account for all these ions in the apatite-crystal structure have proved to be unsuccessful. A recent study shows the general agreement on the substitution of certain ions for others in the structure of apatite.[33] In principle it is possible to substitute Na^+ and Mg^{++} in Ca^{++} positions with provisions made for electrical neutrality when necessary. It is also possible to substitute Cl^- and F^- for the OH^-. Such substitutions, known as isomorphous (same structure) substitutions, can take place in bone apatite but are not always the explanation of the appearance of certain ions in bone mineral. To date no definite proof has been offered to show that carbonate can occupy a position in the apatite structure. Citrate, too, is probably not a structural constituent of apatite but is admixed in some way with the apatite in bone salt.

Another important consideration in the exact nature of bone apatite is the need of an explanation of the lack of ideal apatite stoicheiometry, as shown by chemical analysis. Usually the calcium to phosphorus (molar) ratio is found to be 9/6 as opposed to the theoretic value of 10/6. For this reason, previous references to bone salt in this chapter employed the cautious term *bone apatite*.

Carbonate Problem

The structure of pure hydroxyapatite, as worked out by Mehmel,[20] was given in Figure 3. Whether or not carbonate, in some form, can substitute in the pure apatite structure is of interest because of the presence of carbonate in bone salt. A great deal of attention has been given to the mineral *francolite*, a fluorapatite* containing about 3 per cent CO_2 by weight X-ray diffraction patterns of this material are appreciably the same as fluorapatite. Intensity differences between francolite and fluorapatite, reported earlier,[17] have been shown to be erroneous,[4,30] while the small differences in unit-cell size deduced from the diffraction patterns are not unreasonable considering the impurity of the natural materials studied.[12] No trace of a calcium carbonate or magnesium carbonate phase in untreated francolite has been demonstrated by x-ray diffraction, although it is possible to detect as little as 1 per cent of calcite ($CaCO_3$) admixed with apatite.[39] A lower index of refraction and an increased optical birefringence in francolite as compared to fluorapatite have been reported.[18] This is offered to support the theory that carbonate is substituted in fluorapatite to form francolite.

Calcite lines have been developed in the x-ray patterns of heat-treated francolite.[4] In addition, the lines of CaO were shown superimposed on the apatite after more severe heat treatment.[11] Infrared absorption spectroscopy[31] has shown francolite (as well as dentin, enamel and bone) to exhibit the absorption bands characteristic of calcite and magnesite ($MgCO_3$). Differential solubility tests showing that carbonate is dissolved preferentially by weak acid treatment of this phosphate mineral are also offered as evidence against the substitution of carbonate in the apatite.

In summary, it is felt that although francolite appears to be well crystallized and homogeneous under microscopic examination, it is in fact a multiphase system. The major fluorapatite phase is admixed with very finely divided crystalline (or amorphous) calcite and magnesite, with CaF_2 as a possible trace phase.[4] The experimental methods used on francolite have been applied as well to bone mineral, dentin and enamel. Similar results indicate that the carbonate in these calcified tissues is not substituted in the interior of the apatite crystals. Whether carbonate exists as a separate phase[11] or as a chemisorbed anion linked directly to surface calciums[22] has yet to be decided.

* When all, or most, of the hydroxyl ions of hydroxyapatite are replaced by fluoride ions, the mineral is known as fluorapatite

CRYSTAL SURFACE

The very small crystal size of bone apatite points up the importance of surface reactions in this material. Weikel and Neuman[12] show that 4.52 per cent of the total calcium and 5.47 per cent of the total phosphorus are available for surface exchange in a synthetic apatite with a particle size close to that of bone. If the individual crystals of bone apatite are assumed to be 400 × 300 × 30 A, this would mean about a 4 A surface "skin" containing calcium and phosphorus entering into surface exchange. This represents a tremendous availability of Ca and P when compared with a crystal just ten times as large in each dimension. Assuming the same 4 A penetration for isionic surface exchange, the Ca and the P now exchangeable diminish to 0.045 per cent and 0.055 per cent respectively. Thus, as crystals grow, the importance of the surface layer diminishes.

The extensive studies of the surface chemistry of synthetic-apatite and bone-apatite crystals can only be summarized here. Besides *isionic* exchange, these crystals can undergo surface reactions with ions not present originally in the structure. The ions reportedly replacing surface calcium in *heterionic* surface exchange[26] are uranyl, strontium, sodium and hydronium. Surface phosphate ion is reported to be replaced by carbonate ion,[21] while surface hydroxyl ions can be replaced by fluoride and bicarbonate. Originally the uptake of ions on the surface of bone-apatite crystals was thought to be due to physical adsorption by *van der Waals* bonds. The present view of this uptake is a chemisorption of chemical bonding of certain solution ions to crystal ions on or near the surface. It is not clear whether the citrate ion is adsorbed or bound chemically to surface calcium or whether it is a separate calcium-citrate phase too small to be found by x-ray diffraction.[19]

Another phenomenon that owes its existence to the large surface area in apatite crystals is the layer of water, not held mechanically, which cannot be removed by centrifugation above 40,000 g.[27] This hydration layer can reach a maximum of 80 per cent of the weight of synthetic hydroxyapatite crystals. This high figure is never approached by bone apatite, and generally bone crystals are not so hydrated as the synthetic materials. There is speculation that the bonding between the organic and the crystalline phases of bone prevents the surface addition of this water layer. There is some evidence that this shell acts in such a way as to exclude the passage of certain ions to the crystal surface while allowing others to pass through.[28] The concept of the hydration layer is not fully developed or understood at this writing.

A final concept that stems from the high surface area is the spontaneous recrystallization of both synthetic and bone apatite crystals in an aqueous medium.[23,24] Animal experiments have shown that solution and reprecipitation (i.e., recrystallization) also can take place in vivo.[1,25] Ions that normally are taken up on the surface will become unavailable for further surface exchange with the passage of time. This is illustrated graphically in Figure 7.

In summary, the bone-crystal system may be viewed as (a) the solution, or serum, generally surrounding the crystal; (b) the hydration layer containing nonspecific anions in rapid equilibrium with the solution; (c) the crystal surface containing more or less specific cations and anions also in equilibrium with the solution by way of the hydration layer; and (d) the crystal interior which is in slow but measurable equilibrium with the outer layers (i.e., recrystallization). This is the general view held today by most research workers in the bone-mineral field.[26]

NONSTOICHEIOMETRY IN BONE APATITE

Bone mineral, as well as certain finely divided synthetic and natural calcium phosphates, yields the x-ray diffraction pattern of hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$] but departs from the stoicheiometry of this mineral. In general, chemical analyses show a low Ca/P ratio in these materials. Some workers[13] explained this appa...

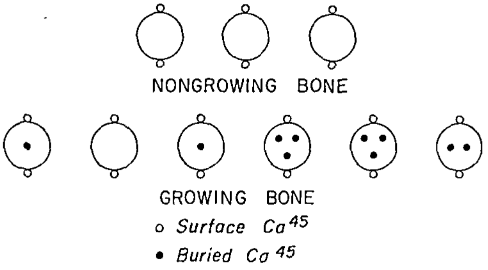


FIG. 7. Illustrating the incorporation of surface Ca^{45} in the center of recrystallized bone crystals. Although growing bone crystals contain more total Ca^{45}, there is less % available on the surface for exchange reactions. (Each large circle represents a single bone crystal.)

stoicheiometry by the existence of adsorbed phosphate (in some form) in the proportion needed to lower the molar Ca/P ratio from ideal 10/6 to the observed figure, which usually was about 9/6. Surface exchange experiments[21] show that low Ca/P apatites do not have excess phosphate-crystal surfaces. Assuming phosphate to be on the surface in excess, it would require a surface area in excess of 100 m^2/g to accommodate all the phosphate needed to lower the Ca/P to 9/6. Nonstoicheiometric apatites with a Ca/P of 9/6 have been prepared with surface areas too low to account for the phosphate adsorption needed to lower the Ca/P ratio to the observed values.[32,34]

Ruling out phosphate adsorption, calcium ions must be missing in some fashion from the apatite structure to reach a low Ca/P ratio. Neuman and Neuman[26] postulate missing calcium ions on the surface of the crystal which are replaced by hydronium (H_3O^+) ions. They suggest that since the surface of bone-apatite crystals is so large a part of the solid, the Ca/P is lowered by this surface nonstoicheiometry.

This theory, too, makes the apatite stoicheiometry a surface area dependent quantity. As mentioned above, nonstoicheiometric apatites have been prepared with specific surfaces too low to explain the change in stoicheiometry solely by the absense of calcium ions on the surface. In addition, apatite crystals would have to be smaller than observed in bone to lower the Ca/P to 9/6 by surface substitution of H_3O^+ for missing calcium and still maintain at least a 4.52 per cent calcium content on the bone surface as reported.[21]

Recent work[32] has provided x-ray diffraction and index of refraction evidence in support of the existence of "calcium-poor" apatites. The calcium ions were shown to be absent statistically from certain positions throughout the synthetic apatite crystals and not only from the surface layer. Electrical neutrality is postulated to be maintained in the crystal by the addition of hydrogen bonding ($2H^+$ for each missing Ca^{++}) between orthophosphate oxygens. A general formula for apatite may be:

$$M_{10-x}H_{2x}(PO_4)_6(OH)_2$$

when M is the sum of the divalent cations (Pb^{+2}, Ca^{+2}, Mg^{+2}, etc.) and H the sum of the monovalent cations, such as H^+ and Na^+. A monovalent cation, such as Na^+, is of the correct order of size for replacing Ca^{++} in the apatite lattice. In this case only one hydrogen is needed for electrical neutrality.

It is very probable that the lack of stoicheiometry in bone apatite can be explained by the mechanism of a calcium-defect apatite structure. Experiments with synthetic "defect" apatites[4,9] show that these compounds can react chemically with calcium in solution, possibly releasing the hydrogen from

the structure. Preliminary experiments by R. C. Likins (National Institute of Dental Research) and the author have shown that the lactic acid solubility of both synthetic apatites and whole teeth (with nonstoicheiometric Ca/P ratios) can be reduced by equilibrating with a calcium-acetate solution. It is not clear what bone functions are dependent upon the missing calcium ions. The density of pure apatite is higher than that of a nonstoicheiometric apatite.[31] In addition, it has been demonstrated that the nonstoicheiometric apatites are more reactive than perfect apatites. Perhaps this reactivity, coupled with the surface properties of bone crystals, defines the behavior of bone crystals in serum.

SOLUBILITY

No solubility product has ever been clearly demonstrated for hydroxyapatite. Results obtained by approaching the solubility from the undersaturated side and from the saturated side invariably disagree.[15,16] It is likely that all attempts in the past to measure the K_{sp} of hydroxyapatite have been made on nonstoicheiometric or mixtures of nonstoicheiometric apatites, since it was only recently[29] that pure apatite was synthesized. The study of the solubility of pure, highly crystalline (i.e., low surface area) hydroxyapatite would be of value. A standard solubility product on a sample of hydroxyapatite would help to evaluate the effect of high surface area and/or impurities on the solubility of hydroxyapatite as it appears in bone.

From solubility-product considerations Neuman and Neuman[26] suggest that bone apatite is formed as a product of the hydrolysis of secondary calcium phosphate ($CaHPO_4$). They cite evidence to show that the simple ion product $Ca \times P_{total}$, rather than $(Ca)^3(PO_4)^2$, or $(Ca)^{10}(PO_4)^6(OH)^2$, seems to correlate with the solubility of apatite in serum. In a recent work Nordin and Meyer[28] report an ion product for bone that is close to that of $CaHPO_4$ at pH 6.6. They suggest that the tissue-fluid concentrations of calcium and phosphate are a result of an equilibrium of the fluid with bone salt having a surface pH of about 6.6.

It seems clear that the ion product of calcium and phosphate in bone-tissue serum is far too high to be accounted for by the solubility of apatite or tertiary calcium phosphate. Both apatite and the tertiary salt are apparently less soluble than the dibasic phosphate. The reason for the apparent "supersaturation" is not fully understood. However, it seems clear that the solubility product of $CaHPO_4$ acts as a limiting factor in the relationship between solid bone and serum.

One must differentiate between bone formation and calcification, or crystal development. The mere precipitation of $CaHPO_4$ or $Ca_{10}(PO_4)_6(OH)_2$ crystals from solution is only one step in the process of tissue formation. Further solubility studies may lead to the understanding of the major process—bone growth—as well as the precipitation of bone salt necessary for the tissue growth.

CONCLUSIONS

Many important contributions to the understanding of bone mineral have been omitted from this discussion for reasons of clarity and brevity. Such problems as the study of bone mineral as an alkali reserve, the role of the citrate ion found in conjunction with bone mineral, the mechanism of calcification, the better understanding of ions known as bone seekers, are barely mentioned in the foregoing discussion. Many questions remain to be answered; much is waiting to be discovered in regard to the structure and the function of bone mineral.

In this chapter I have chosen to give background in crystal chemistry to help understand the arguments arising from the study of bone crystals and their mineral and synthetic counterparts. The importance of crystal size in the role of bone apatite and the present views on the actual structure of bone crystals were thoroughly discussed. The present hypotheses of bone-mineral st-

ture serve only as a springboard for further work. As pointed out by A. E. Sobel at the 1956 Gordon Research Conference on The Structure, Chemistry and Physiology of Bones and Teeth, the true value of a scientific hypothesis is the resulting experiment which can be designed to test its validity.

REFERENCES

1. Bavetta, L., and Likins, R. C.: Personal communication.
2. Bertaut, M. F.: Compt. rend. Acad. sc. 228:492, 1949.
3. Bunn, C. W.: Chemical Crystallography, London, Oxford, 1945.
4. Carlström, D.: Acta radiol., Supp. 121, 1955.
5. Dallemagne, M., Fabry, C., and Posner, A. S.: J. physiol., Paris, 46:325, 1954.
6. DeJong, W. F.: Rec. trav. chim. 45:445, 1926.
7. Engström, A., and Finean, J. B.: Nature 171:564, 1953.
8. Fabry, C.: Biochim. et biophys. acta 14: 401, 1954.
9. ———: J. physiol., Paris, 46:361, 1954.
10. Finean, J. B., and Engström, A.: Biochim. et biophys. acta 11:178, 1953.
11. Geiger, T.: Schweiz. Mineralog. Petrog. Mitt. 30:161, 1950.
12. Hendricks, S. B.: Tr. 4th Conf. on Metabolic Interrelations, New York, Macy, 1952.
13. Hendricks, S. B., and Hill, W.: Proc. Nat. Acad Sc. U.S. 36:731, 1950.
14. Klug, H., and Alexander, L. E.: X-ray Diffraction Procedures, New York, Wiley, 1954.
15. Kuyper, A. G: J. Biol Chem. 159:411, 1945.
16. Levinskas, G J.: Thesis, Univ. of Rochester, 1953.
17. McConnell, D: Bull. Soc. fr. min. et crist 75:428, 1952.
18. ———: Tr. 4th Conf. on Metabolic Interrelations, New York, Macy, 1952.
19. McLean, F. C., and Urist, M. R.: Bone, An Introduction to the Physiology of Skeletal Tissue, Chicago, Univ. Chicago Press, 1955.
20. Mehmel, M.: Ztschr. Krist. 75:323, 1930.
21. Neuman, W. F.: Atomic Energy Report UR-238, 1953.
22. ———: J. Am. Chem. Soc. 77:317, 1955.
23. Neuman, W. F., and Mulryan, B. J.: J. Biol. Chem. 185:705, 1950.
24. ———: J. Biol. Chem. 193:237, 1951.
25. ———: J. Biol. Chem. 195:842, 1952.
26. Neuman, W. F., and Neuman, M. W.: Chem. Rev. 53:1-45, 1953.
27. Neuman, W. F., Toribara, T. Y., and Mulryan, B. J.: Atomic Energy Report UR-230, 1952.
28. Nordin, B. E. C., and Meyer, K.: Personal communication.
29. Perloff, A., and Posner, A. S.: Science 48: 383, 1956.
30. Posner, A. S.: Thesis, Univ. of Liége, 1954.
31. Posner, A. S., and Duyckaerts, G.: Experientia 10:424, 1954.
32. Posner, A. S., and Perloff, A.: J. Res. Nat. Bur. Stds., May, 1957.
33. Posner, A. S., and Stephenson, S. R.: J. Am. Dent. A. 46:257, 1953.
34. ———: J. Dent. Res 31:371, 1952.
35. Robinson, R. A.: Personal communication.
36. Robinson, R. A., and Watson, M. L.: Anat. Rec. 114:383, 1952.
37. ———: Ann. New York Acad. Sc. 60: 596, 1952.
38. Stoll, W. R.: Thesis, Univ. of Rochester, 1956.
39. Tovborg-Jensen, A.: Acta odont. scandinav. 6:7, 1944.
40. Tovborg-Jensen, A., and Moller, A.: J. Dent. Res. 27:524, 1948.
41. Warren, B. E., and Averbach, B. L.: J. Appl. Physiol. 21:595, 1950.
42. Weikel, J. H., and Neuman, W. F.: Atomic Energy Report UR-228, 1952.

Le Structura de Mineral Ossee

Summario in Interlingua

Iste articulo es un revista critic del litteratura currente super le crystallochimia de mineral ossee. Es includite in le introduction un breve discussion del theoria crystallochimic. Un section del articulo discute le methodos disveloppate pro determinar le dimensiones del crystallos de mineral ossee. Es reportate le resultatos obtenibile per

technicas como le microscopia electronic, le diffraction de radios X, e le adsorption nitrogenic a basse temperaturas. Studios del structura crystallin de mineral ossee e de simile minerales apatitic es discutite in detalio. Le problemas de substitution isomorphe, de inclusion de carbonato, e de non-stoichiometria es analysate in le systemas apatitic e in le histos calcificate mesme. Le section final se occupa del studios reportate in re le solubilitate de mineral ossee e de simile minerales apatitic.

ture serve only as a springboard for further work. As pointed out by A. E. Sobel at the 1956 Gordon Research Conference on The Structure, Chemistry and Physiology of Bones and Teeth, the true value of a scientific hypothesis is the resulting experiment which can be designed to test its validity.

REFERENCES

1. Bavetta, L., and Likins, R. C.: Personal communication.
2. Bertaut, M. F.: Compt. rend. Acad. sc. 228:492, 1949.
3. Bunn, C. W.: Chemical Crystallography, London, Oxford, 1945.
4. Carlström, D.: Acta radiol., Supp 121, 1955.
5. Dallemagne, M., Fabry, C, and Posner, A. S.: J. physiol., Paris, 46:325, 1954.
6. DeJong, W. F.: Rec. trav. chim. 45:445, 1926.
7. Engström, A., and Finean, J. B.: Nature 171:564, 1953.
8. Fabry, C.: Biochim. et biophys. acta 14: 401, 1954.
9. ———: J. physiol., Paris, 46:361, 1954.
10. Finean, J. B., and Engström, A.: Biochim. et biophys acta 11:178, 1953.
11. Geiger, T.: Schweiz. Mineralog. Petrog. Mitt. 30:161, 1950.
12. Hendricks, S. B.: Tr. 4th Conf. on Metabolic Interrelations, New York, Macy, 1952.
13. Hendricks, S. B, and Hill, W.: Proc. Nat. Acad. Sc. U.S. 36:731, 1950
14. Klug, H., and Alexander, L. E.: X-ray Diffraction Procedures, New York, Wiley, 1954.
15. Kuyper, A. G.: J. Biol. Chem. 159:411, 1945.
16. Levinskas, G. J.: Thesis, Univ. of Rochester, 1953.
17. McConnell, D.: Bull. Soc. fr. min. et crist 75:428, 1952.
18. ———: Tr. 4th Conf. on Metabolic Interrelations, New York, Macy, 1952.
19. McLean, F. C., and Urist, M. R.: Bone, An Introduction to the Physiology of Skeletal Tissue, Chicago, Univ. Chicago Press, 1955.
20. Mehmel, M.: Ztschr. Krist. 75:323, 1930.
21. Neuman, W. F.: Atomic Energy Report UR-238, 1953.
22. ———: J. Am. Chem. Soc. 77:317, 1955.
23. Neuman, W. F., and Mulryan, B. J.: J. Biol. Chem. 185:705, 1950.
24. ———: J. Biol. Chem. 193:237, 1951.
25. ———: J. Biol. Chem. 195:842, 1952.
26. Neuman, W. F., and Neuman, M. W.: Chem. Rev. 53:1-45, 1953.
27. Neuman, W. F., Toribara, T. Y., and Mulryan, B. J.: Atomic Energy Report UR-230, 1952.
28. Nordin, B. E. C., and Meyer, K.: Personal communication.
29. Perloff, A., and Posner, A. S.: Science 48: 383, 1956.
30. Posner, A. S.: Thesis, Univ. of Liége, 1954.
31. Posner, A. S., and Duyckaerts, G.: Experientia 10:424, 1954.
32. Posner, A. S., and Perloff, A.: J. Res. Nat. Bur. Stds., May, 1957.
33. Posner, A. S., and Stephenson, S. R.: J. Am. Dent. A. 46:257, 1953.
34. ———: J. Dent. Res. 31:371, 1952.
35. Robinson, R. A.: Personal communication.
36. Robinson, R. A., and Watson, M. L.: Anat. Rec. 114:383, 1952.
37. ———: Ann New York Acad. Sc. 60: 596, 1952.
38. Stoll, W. R.: Thesis, Univ. of Rochester, 1956.
39. Tovborg-Jensen, A.: Acta odont scandinav. 6:7, 1944.
40. Tovborg-Jensen, A., and Moller, A.: J. Dent. Res. 27:524, 1948.
41. Warren, B. E., and Averbach, B. L.: J. Appl Physiol. 21:595, 1950.
42. Weikel, J. H., and Neuman, W. F.: Atomic Energy Report UR-228, 1952.

Le Structura de Mineral Ossee

Summario in Interlingua

Iste articulo es un revista critic del litteratura currente super le crystallochimia de mineral ossee. Es includite in le introduction un breve discussion del theoria crystallochimic Un section del articulo discute le methodos disveloppate pro determinar le dimensiones del crystallos de mineral ossee. Es reportate le resultatos obtenibile per

technicas como le microscopia electronic, le diffraction de radios X, e le adsorption nitrogenic a basse temperaturas. Studios del structura crystallin de mineral ossee e de simile minerales apatitic es discutite in detalio. Le problemas de substitution isomorphe, de inclusion de carbonato, e de non-stoichiometria es analysate in le systemas apatitic e in le histos calcificate mesme. Le section final se occupa del studios reportate in re le solubilitate de mineral ossee e de simile minerales apatitic.

3

The Organic Matrix of Bone and Epiphyseal Cartilage*

ROBERT A. ROBINSON, M.D., AND D. A. CAMERON, M.D.S.†

INTRODUCTION

Occasionally the idea is expressed, perhaps carelessly, that when cartilage calcifies bone is formed. This, of course, is not true. Since calcification is a normal function of bone and some cartilage matrices, one cannot discuss the organic matrix without considering the manner in which it calcifies.

When cartilage matrix calcifies, the cells in the region of calcification are undergoing changes that end eventually in their dissolution. The cells in cartilage have no apparent canaliculi that connect them together, and they are believed to receive nutrient via perfusion through their highly hydrated matrix from paravascular spaces on the periphery of the cartilage mass (Fig. 1). However, it is doubtful that nutrient in sufficient amount can perfuse to the cells when their matrix is calcified.[11] The suggestion is that the inorganic crystals replace something in the matrix, perhaps the cement substance water, without expanding the total matrix volume, and thus the transport of nutrient to the cells is interrupted.[20,22] The capsule about the cartilage cells should be noted. In the matrix closely bordering this

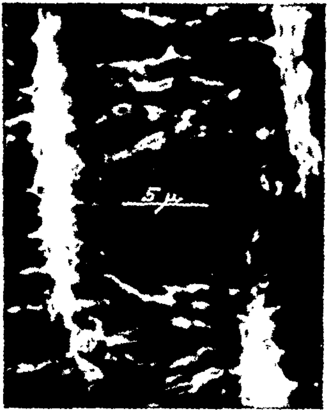
* From the Division of Orthopaedic Surgery, The Johns Hopkins University Medical School, Baltimore, Maryland. The investigations of the authors referred to in this paper were supported by the U. S. Public Health Service, National Institutes of Health, through research grant A-706-C (Arthritis and Metabolic Diseases) and research grant A-909-C (Metabolism and Nutrition).

† Supported by grants under the Fulbright and U. S. Information and Education Exchange (Smith-Mundt) Acts.



FIG. 1. Electron micrograph of cartilage from the proliferative zone of the distal end of the femur of a newborn infant. Note the capsular region about each cell. Between the capsules the matrix contains a quantity of tiny fibrils. All the material for electron micrography was stained and fixed with osmium textroxide and embedded in a mixture of butyl and methyl methacrylate. Sections were made with a glass knife on a Porter-Blum microtome.[20]

FIG. 2. Photographically enlarged light micrograph of bone. The lacunae and the cannaliculi are well seen. The fact that the cells and the lacunae occupy a large percentage of the volume of this bone specimen is evident. The matrix is black. (Robinson, R. A.: J. Bone & Joint Surg. 31A: 398)



capsule or "moat," Brower[4] found "chloride" localization. (The "capsule" or "moat" may be an artefact, occurring particularly during fixation of degenerating cartilage cells.)

When bone matrix calcifies, the cells in the region of calcification remain viable. The cells in bone tissue (osteocytes) and around a mass of bone tissue (osteoblasts) are connected with one another by canaliculi. In newly forming bone at least, protoplasmic extensions of these cells pervade the



FIG 3. Electron micrograph of decalcified bone (A) Part of cytoplasm. (B) Collagenous matrix. (C) Cytoplasmic extension into lacuna The details of the collagen fibrils in the matrix are not well resolved, as in Figure 9.

canaliculi (Figs. 2 & 3). The cells in the center of a mass of bone tissue appear thus to be part of a multinucleated protoplasmic network. Some investigators hold the concept that in the anabolic phase the interstices of this network of bone cells (osteoblasts covering the periphery and osteocytes strung out spiderlike in the center of the bone mass) are filled by matrix. In the catabolic phase the extracytoplasmic matrix is resorbed while the cytoplasm of bone cells coalesces to form multinucleated cellular masses. These multinucleated cell masses break up into osteoclasts of various dimensions. As observed by time-lapse movies in tissue culture of skull bone of the mouse which is under parathyroid hormone stimulation, these osteoclasts obviously move about freely in the bone specimens,[10] whereas osteocytes and osteoblasts in tissue culture are relatively sessile.

If the environment of the bone cells then changes again so that the cells become associated with matrix production, they are believed to assume a uninuclear form. However, in this state the protoplasm associated with each osteoblast nucleus is connected by cytoplasmic bridges as the cell becomes an osteocyte. It is now thought that nutrition reaches the bone cells living in the center of a bone mass via the canaliculi when perfusion of nutrients to the bone matrix is obstructed by matrix calcification. It is interesting in this relationship to note that Ham[11] found that bone cells in the radius of the dog were rarely farther than 0 25 mm. from a vascular supply, as, for instance, from the vessel in a haversian canal: most cells were within 0.1 mm. of a capillary. Thus this canalicular system has its limitations as a nutrient transport mechanism.

The bulk of the mineral component of both bone and calcified epiphyseal cartilage is deposited in essentially the same form: extremely short, tabular-shaped crystals of hydroxyapatite.*

---

* The habit, or shape, and the size of bone crystals have been observed in electron micrographs of disintegrated bone and bone sections.[20,23,24,26] These have been compared with crystals from disintegrated enamel and sectioned enamel and dentin[19,27] and with apatite crystals developing in vitro.[28]

1. The habit of bone crystals: thin tablets. From the physiological standpoint the length is not believed to be so important as crystal thickness[24] The thickness of these thin tablets is about 25 to 75 A, whereas the thickness of the ribbons of apatite seen in *enamel* is about 100 A[27]

2. The length of the bone crystals. They range in longest dimensions all the way from the smallest speck resolvable by the electron microscope being used (about 25 A) to about 1,500 A. However, none of the crystals so far observed is 2,500 A or longer; therefore, none of them would be visible in the *light microscope.*

3 Average size of bone crystals In a study of the crystal sizes in subperiosteal rib bone from a young adult, two distinct peaks are found in a distribution curve, one peak about 180 A and another about 400 A -[!] The peak at 180 A for crystal length was about four times as high as the one at 400 A in the distribution curve. In general, the width and the length of the smaller crystals were comparable Electron diffraction studies on sections of calcified bone suggest that even these smaller crystals which have no apparent long axis probably have [illegible] "C" axis parallel to the long axis of the coll[illegible]n fibril with which they are asso- [illegible]

near enough to a collagen fibril in bone matrix so that this correlation can be observed

In the bone from an aged individual (bone which is considered to be of long standing)—the crystal length was as great as 1,500 A in such specimens—the average crystal length was greater than in specimens from bone which was believed to be newly formed. Schwarz and Pahlke[26] also noted what appeared to be longer crystals in longer established bone.

No fixed length for bone crystals has been set from electron micrograph observations, since these observations consist of spot checks from bone procured from various sites and prepared in various ways. In those preparation methods involving temperatures above 37° C., crystal size is perhaps distorted by crystal growth[24] Certainly after treatment at 600° C. the crystals tend to meld into longer crystals which have a very definite hexagonal or octagonal outline but are so thick that they do not allow transmission of electrons in the electron microscope we have used[10]

Electron micrographs have demonstrated variability in bone-crystal length within the 25 A to 1,500 A range. The average length varies in different samples. For purposes of calculating isotope exchange, it appears that thickness, or rather the smallest dimension, of the crystal is probably the most important one by far.[24]

Of course other inorganic matter such as sodium, chloride, potassium and magnesium is present in the cells or in the matrix, but in a fully calcified specimen of either epiphyseal cartilage or bone this portion of the mineral component is relatively small.[8] The CO_2 associated with these structures is thought to be largely present as a carbonate and exchangeable as such with phosphate ions around and in the surface layers of apatite crystals.

Opinion today is that the organic matrices of epiphyseal cartilage, dentin and bone which normally calcify are chemically constructed so that they can concentrate phosphate and calcium atoms to the point where a calcium-phosphate crystal will form. The cytoplasm of osteoblasts and osteocytes, odontoblasts and cartilage cells do not calcify. Inorganic crystals have not been observed in these cells. Ameloblasts according to Watson and Avery[27] probably have cytoplasmic calcification, but this occurs only in ameloblasts in a specialized part of the cytoplasm and does not normally involve all the cytoplasm of an ameloblast. Actual points at which this concentration of phosphate and calcium in the bone and dentin matrices, and probably in epiphyseal cartilage matrix, occurs is on or very near the surface of, and possibly inside, collagen fibrils.[21,27] It appears that the crystal-formation sites may be associated not only with the collagen fibril but with a specific region of the fibril. To Robinson and Watson[23] it appeared that in bone matrix this region was associated with the more dense bands in the collagen.

After the first crystals are formed, unless a mineral deficit is present in the whole organism (e.g., rickets), the cement substance around the fibrils fills with crystals. The fact that hydroxyapatite is the most stable form of a calcium-phosphate crystal in the pH range of mammalian tissues may be the determining factor that causes all intrasomatic calcifications in man to be composed of hydroxyapatite crystals or crystals of a very similar apatite lattice structure.[3] In other words, calcification is thought to be due to a specific quality of the organic matrix of calcifying tissue. Avery and Watson set forth a present-day concept as follows:[27]

> Neuman and Neuman[15] and DiStefano *et al.*[7] have suggested that calcification in bone and cartilage is probably initiated by a change in the organic matrix such that it presents ions bound to the protein in a pattern like that of the hydroxyapatite lattice. This lattice of organically bound ions then acts as a seed on which calcification can commence. Crystals formed on such a seed will be strictly oriented by, and will follow, the orientation of the matrix molecules. Such a model explains rather satisfactorily how the crystals of bone and enamel and presumably dentine can be so well oriented with respect to the organic matrices of collagen and eukeratin.

Despite their similar ability to become loaded with inorganic crystals, the organic matrices of epiphyseal cartilage and bone have a very different appearance in the electron microscope, and the course of calcification in them is not identical. Furthermore, "normal" bone and cartilage matrices may show variations in structure, depending on their site and age. The study of the end of a long bone from a newborn infant has provided evidence that even the components of cartilage at the joint surface differ in their organization from those in the near-by epiphyseal cartilage, and that the organic component organization in both differs from that in bone.[5,20]

CARTILAGE MATRIX

In the newborn infant, cartilage matrix from the distal femoral epiphyseal line[20] has been found to differ from that at the articular surface. The main difference is in the number of fibrils in a given volume of matrix and in the thickness or the diameter of the fibrils. At the articular surface the fibrils are about 250 to 500 A in diameter and are grouped into bundles that form the collagen fibers seen with the light microscope. These fibril bundles are found only in a narrow band at the joint surface. In the rest of the epiphysis the fibrils have little

canaliculi (Figs. 2 & 3). The cells in the center of a mass of bone tissue appear thus to be part of a multinucleated protoplasmic network. Some investigators hold the concept that in the anabolic phase the interstices of this network of bone cells (osteoblasts covering the periphery and osteocytes strung out spiderlike in the center of the bone mass) are filled by matrix. In the catabolic phase the extracytoplasmic matrix is resorbed while the cytoplasm of bone cells coalesces to form multinucleated cellular masses. These multinucleated cell masses break up into osteoclasts of various dimensions. As observed by time-lapse movies in tissue culture of skull bone of the mouse which is under parathyroid hormone stimulation, these osteoclasts obviously move about freely in the bone specimens,[10] whereas osteocytes and osteoblasts in tissue culture are relatively sessile.

If the environment of the bone cells then changes again so that the cells become associated with matrix production, they are believed to assume a uninuclear form. However, in this state the protoplasm associated with each osteoblast nucleus is connected by cytoplasmic bridges as the cell becomes an osteocyte. It is now thought that nutrition reaches the bone cells living in the center of a bone mass via the canaliculi when perfusion of nutrients to the bone matrix is obstructed by matrix calcification. It is interesting in this relationship to note that Ham[11] found that bone cells in the radius of the dog were rarely farther than 0.25 mm. from a vascular supply, as, for instance, from the vessel in a haversian canal: most cells were within 0.1 mm. of a capillary. Thus this canalicular system has its limitations as a nutrient transport mechanism.

The bulk of the mineral component of both bone and calcified epiphyseal cartilage is deposited in essentially the same form: extremely short, tabular-shaped crystals of hydroxyapatite.*

---

* The habit, or shape, and the size of bone crystals have been observed in electron micrographs of disintegrated bone and bone sections.[20,23,24,25] These have been compared with crystals from disintegrated enamel and sectioned enamel and dentin[19,27] and with apatite crystals developing in vitro.[23]

1. The habit of bone crystals: thin tablets. From the physiological standpoint the length is not believed to be so important as crystal thickness.[24] *The thickness of these thin tablets is about 25 to 75 A*, whereas the thickness of the ribbons of apatite seen in *enamel* is about 100 A.[27]

2. The length of the bone crystals. They range in longest dimensions all the way from the smallest speck resolvable by the electron microscope being used (about 25 A) to about 1,500 A. However, none of the crystals so far observed is 2,500 A or longer; therefore, none of them would be visible in *the light microscope.*

3. Average size of bone crystals. In a study of the crystal sizes in subperiosteal rib bone from a young adult two distinct peaks are found in a distribution curve: one peak about 180 A and another about 400 A.[23] The peak at 180 A for crystal length was about four times as high as the one at 400 A in the distribution curve. In general, the width and the length of the smaller crystals were *comparable. Electron diffraction studies on sections* of calcified bone suggest that even these smaller crystals which have no apparent long axis probably have their "C" axis parallel to the long axis of the collagen fibril with which they are associated.[23] The longer crystals, about 400 A and over, *have a visible long axis, and then it is obvious that* the crystal and the collagen axes are almost parallel, or exactly parallel, at least where the crystals are near enough to a collagen fibril in bone matrix so that this correlation can be observed.

In the bone from an aged individual (bone which is considered to be of long standing)—the crystal length was as great as 1,500 A in such specimens—the average crystal length was greater than in speci*mens from bone which was believed to be newly* formed. Schwarz and Pahlke[26] also noted what appeared to be longer crystals in longer established bone.

No fixed length for bone crystals has been set from electron micrograph observations, since these observations consist of spot checks from bone procured from various sites and prepared in various ways. In those preparation methods involving tem*peratures above 37° C., crystal size is perhaps dis*torted by crystal growth.[24] Certainly after treatment at 600° C. the crystals tend to meld into longer crystals which have a very definite hexagonal or octagonal outline but are so thick that they do not allow transmission of electrons in the electron microscope we have used.[10]

Electron micrographs have demonstrated variability in bone-crystal length within the 25 A to *1,500 A range. The average length varies in differ*ent samples. For purposes of calculating isotope exchange, it appears that thickness, or rather the smallest dimension, of the crystal is probably the most important one by far.[24]

Of course other inorganic matter such as sodium, chloride, potassium and magnesium is present in the cells or in the matrix, but in a fully calcified specimen of either epiphyseal cartilage or bone this portion of the mineral component is relatively small.[8] The CO_2 associated with these structures is thought to be largely present as a carbonate and exchangeable as such with phosphate ions around and in the surface layers of apatite crystals.

Opinion today is that the organic matrices of epiphyseal cartilage, dentin and bone which normally calcify are chemically constructed so that they can concentrate phosphate and calcium atoms to the point where a calcium-phosphate crystal will form. The cytoplasm of osteoblasts and osteocytes, odontoblasts and cartilage cells do not calcify. Inorganic crystals have not been observed in these cells. Ameloblasts according to Watson and Avery[27] probably have cytoplasmic calcification, but this occurs only in ameloblasts in a specialized part of the cytoplasm and does not normally involve all the cytoplasm of an ameloblast. Actual points at which this concentration of phosphate and calcium in the bone and dentin matrices, and probably in epiphyseal cartilage matrix, occurs is on or very near the surface of, and possibly inside, collagen fibrils.[24,27] It appears that the crystal-formation sites may be associated not only with the collagen fibril but with a specific region of the fibril. To Robinson and Watson[23] it appeared that in bone matrix this region was associated with the more dense bands in the collagen.

After the first crystals are formed, unless a mineral deficit is present in the whole organism (e.g., rickets), the cement substance around the fibrils fills with crystals. The fact that hydroxyapatite is the most stable form of a calcium-phosphate crystal in the pH range of mammalian tissues may be the determining factor that causes all intrasomatic calcifications in man to be composed of hydroxyapatite crystals or crystals of a very similar apatite lattice structure.[3] In other words, calcification is thought to be due to a specific quality of the organic matrix of calcifying tissue. Avery and Watson set forth a present-day concept as follows:[27]

> Neuman and Neuman[15] and DiStefano *et al.*[7] have suggested that calcification in bone and cartilage is probably initiated by a change in the organic matrix such that it presents ions bound to the protein in a pattern like that of the hydroxyapatite lattice. This lattice of organically bound ions then acts as a seed on which calcification can commence. Crystals formed on such a seed will be strictly oriented by, and will follow, the orientation of the matrix molecules. Such a model explains rather satisfactorily how the crystals of bone and enamel and presumably dentine can be so well oriented with respect to the organic matrices of collagen and eukeratin.

Despite their similar ability to become loaded with inorganic crystals, the organic matrices of epiphyseal cartilage and bone have a very different appearance in the electron microscope, and the course of calcification in them is not identical. Furthermore, "normal" bone and cartilage matrices may show variations in structure, depending on their site and age. The study of the end of a long bone from a newborn infant has provided evidence that even the components of cartilage at the joint surface differ in their organization from those in the near-by epiphyseal cartilage, and that the organic component organization in both differs from that in bone.[5,20]

CARTILAGE MATRIX

In the newborn infant, cartilage matrix from the distal femoral epiphyseal line[20] has been found to differ from that at the articular surface. The main difference is in the number of fibrils in a given volume of matrix and in the thickness or the diameter of the fibrils. At the articular surface the fibrils are about 250 to 500 A in diameter and are grouped into bundles that form the collagen fibers seen with the light microscope. These fibril bundles are found only in a narrow band at the joint surface. In the rest of the epiphysis the fibrils have little

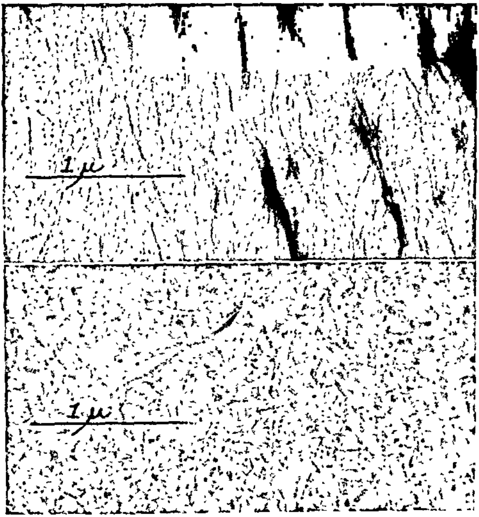


FIG. 4. *(Top)* Electron micrograph of epiphyseal cartilage matrix. This section came from the precalcification zone of the epiphyseal cartilage region of the distal end of the newborn human femur. Only a tendency toward fiber formation (bundles of parallel fibrils) is observed. The fibrils are very narrow and are loosely packed. *(Bottom)* Electron micrograph of cartilage matrix from the distal femur of the puppy near, but not at, the joint surface. Note the assortment of large and small fibrils and the lack of any parallel-running bundles of fibrils. Staining of collagen bands by the osmic acid fixative is observed only in the larger fibrils. (*Top* Robinson & Cameron: J. Biophysic. & Biochem. Cytol, Vol. 2, Supp. No. 4)

tendency to run in bundles and are mostly thinner (50 to 250 A in diameter), and in these areas it has *not* been possible for the authors to stain the periodic structure of the fibrils so that fibril bands could be resolved in the electron microscope as in the case of the fibrils in the articular layer of cartilage or in bone (Fig. 4).

Cartilage matrix from subsurface layers of articular cartilage in a puppy show fibrils of varying size, widely dispersed in the cement substance as compared with bone fibrils and running in every direction without evidence of fiber formation (Fig. 4).

The fibrils in costocartilage from the newborn child reported by Zbinden[29] vary in thickness from 200 to 1,200 A. This is greater than the range of 250 to 500 A which we observed in the surface layers of the newborn human femoral articular cartilage, where the fibrils were larger than in the near-by epiphyseal cartilage. In the rib Zbinden shows that the fibrils have obvious cross striations: they form a loose but regularly arranged network; run straight without branching; and do not group into bundles or fibers. In the costal cartilage of aged subjects Zbinden shows that the fibrils are still within the range of diameter noted in the same cartilage of newborns, but a greater percentage have a larger diameter. According to this author, there is no longer a regular network of straight fibrils, but instead they are grouped into coarse bundles, and adjacent fibrils tend to have their cross striations in phase. In between the bundles of fibrils the fibrils take an irregular course.

In electron micrographs, epiphyseal cartilage matrix appears to be largely cement substance from a volume standpoint. Partridge[17] analyzed bovine nasal cartilage. He found that this cartilage was composed of two major components—chondroitin sulfate and collagen. This cartilage probably has



FIG. 5. An electron micrograph of a vertical column of calcifying cartilage matrix from the epiphyseal line. Figure 6 comes from a region such as that marked (A). Figure 7 comes from a region such as that marked (B). It will be noted that this epiphyseal cartilage calcification begins spottily over a wide area compared with bone (Fig. 10), and that the calcification begins neither at the edge of the cartilage cell capsules (C) nor in the center of the matrix column but between these two points on either side of the column. Part of a cell is included in the section (D). (Robinson & Cameron: J. Biophysic. & Biochem. Cytol., Vol. 2, Supp. No. 4)

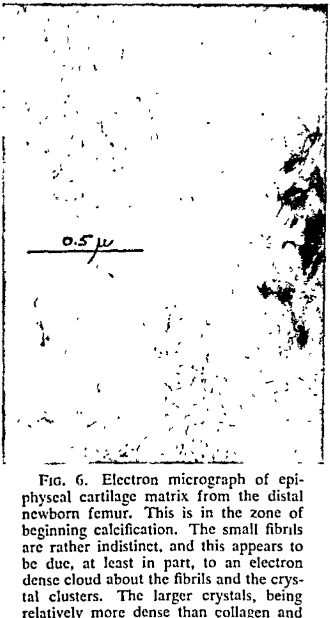


FIG. 6. Electron micrograph of epiphyseal cartilage matrix from the distal newborn femur. This is in the zone of beginning calcification. The small fibrils are rather indistinct, and this appears to be due, at least in part, to an electron dense cloud about the fibrils and the crystal clusters. The larger crystals, being relatively more dense than collagen and more dense than this cloud or haze, are seen rather distinctly as short dark lines. In some places these lines in this micrograph seem to be oriented parallel to the small collagen fibrils. (Robinson & Cameron: J. Biophysic. & Biochem Cytol, Vol. 2, Supp. No. 4)

larger fibrils and more fibrils per unit area than epiphyseal cartilage, but his conclusions as to the chemical composition of cartilage and his speculations about the probable cross linkages between the mucopolysaccharide and the collagen are of interest. Eichelberger, Brower and Roma have studied the inorganic constituents of hyaline cartilage.[8]

CALCIFICATION OF EPIPHYSEAL CARTILAGE MATRIX

This is a normal process in epiphyseal cartilage, or it may occur in other cartilage matrices as the tissue ages. In both cases it accompanies the dissolution of the cells. Epiphyseal cartilage calcifies before it is replaced by bone at the epiphyseal line. In the epiphysis at the distal end of the femur of the newborn infant we observe the earliest sign of calcification of cartilage matrix about the level of the third cartilage cell capsule just distal to the epiphyseal line (Fig. 5). Single crystals measuring from a speck (about 25 Å or the lower limit of the resolution of the electron microscope being used) to 750 Å in length by about 25 to 75 Å in



FIG. 7. The material is prepared in the same way and the site is about the same as that in Figure 6. The magnification is about half of that in Figure 6. In the larger clusters there is no evidence that the crystals are oriented in relation to fibrils, since most of the fibrils are running in the direction of the long axis of the biggest oval collection of crystals, while the longer crystals on the periphery of this cluster appear to be radially arranged about the center of the cluster. However, in the smallest of the three inorganic crystal clusters there appears to be a definite concentration of the inorganic densities along the small fibrils, which one may observe running into and out of this particular calcification center. Certainly there is some evidence that the crystals start to form about the fibrils, but there is none that, as crystallization extends through the cement substance from a calcification center of epiphyseal cartilage, a co-orientation of crystal and fibril long axes is present.

thickness are seen (Fig. 6). At crystal-inception points several crystals may be surrounded by a cloud in the cement substance space about fibrils. This cloud is not so dense as the crystals but more dense than the cement substance. This cloud may be a



FIG. 8 Electron micrograph of fully calcified epiphyseal cartilage. On the left is a segment of the capsule of a hypertrophic cartilage cell. There is no calcification about the small fibrils in the periphery of the cell capsule. The long axes of the longer crystals can be seen going in every direction. Nowhere does one observe the periodic (about 630 A) concentration of inorganic densities that is so typical of bone (cf. Fig. 11). (Robinson & Cameron. J. Biophysic. & Biochem. Cytol., Vol. 2, Supp. No. 4)

concentration of inorganic material in the cement substance not yet crystallized, or it may be made up of crystal units which are not large enough to be resolved by the electron microscope (Fig. 6). As small clusters of crystals develop in these calcification foci, only in rare instances do they appear to lie in such a way that their long axis parallels a long fibril axis (Fig. 6) and that only at the beginning of the calcification process. As crystal clusters expand, the peripheral crystals appear radially arranged and without any clear spatial relationship to fibrils in the area (Fig. 7). The inorganic crystals in epiphyseal cartilage matrix certainly spread through and fill the cement substance about the fibrils.

Although on the basis of electron-micrograph studies on bone and dentin it seems to be clear that the first crystals form at a fibril-cement substance interface or even in the fibril between its polypeptide chains, a demonstration of this same mechanism in the electron micrographs of epiphyseal cartilage

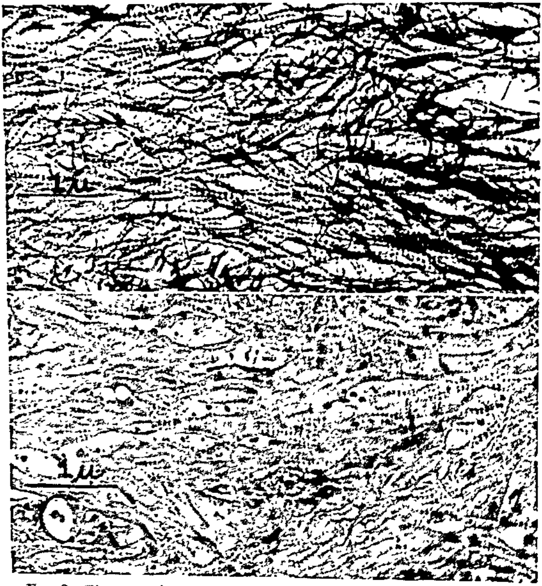


Fig. 9. Electron micrograph of bone matrix decalcified in versene from a newborn infant *(top)* and from a comparable site in an 80-year-old man *(bottom)*. The magnifications in the two micrographs are comparable. The fibrils are larger and more closely packed in the bone from the elderly man. However, in both instances the collagen fibrils are larger and more closely packed in bone than in any of the cartilage at the distal end of the femur of the newborn infant which we have observed. (Robinson & Watson: Ann. New York Acad. Sc. 60:607 & 614)



FIG. 10. Electron micrograph of calcifying osteoid in the metaphyseal region of a newborn infant immediately proximal to the distal femoral epiphyseal line. At the top one sees a little segment of an osteoblast's cell membrane and cytoplasm (A). The collagen fibrils of the uncalcified osteoid are observed in region (B). The earliest calcification is observed in clusters (C). These crystals appear not only to surround fibrils but in some instances to permeate the fibrils with which they are associated. Again a haze, or cloud, is noted about the crystallization centers. The long crystal axes are observed in some places to parallel a fibril axis. (Robinson & Cameron: J. Biophysic. & Biochem. Cytol., Vol. 2, Supp. No. 4)

is not so convincing but is suggested (Figs. 6 & 7), i.e., they form next to fibrils.

The clusters of crystals increase in size and coalesce until all except the center of the cartilage-matrix column at the epiphyseal line and a few fibrils at the edge of the cartilage-cell capsules are calcified (Figs. 5 & 8). No reorganization of the fibrils occurs after calcification, as the fibril pattern in decalcified epiphyseal cartilage is the same as that prior to calcification.[20] The calcification in old age is probably a degenerative process. Zbinden described the process in the costal cartilage of older subjects and noted that clusters of cyrstals were related to the fibrils in this material exactly as the authors found in the epiphyseal cartilage.

In newly formed bone tissue in the metaphysis adjacent to the epiphyseal line, where the comparison can easily be made, calcified cartilage can be seen to differ from calcified bone mainly in the lack of any areas in which there is obvious crystal-collagen coorientation (see Fig. 11).

BONE MATRIX

Whereas epiphyseal cartilage appears in electron micrographs to be largely cement substance containing a loose network of small-diameter collagen fibrils, bone matrix appears to be largely collagen fibrils of greater diameter with a comparatively smaller cement-substance space (Fig. 9). The fibrils of bone matrix (osteoid) are *larger in diameter than those in epiphyseal* cartilage matrix, and their cross striations are easily stained. The striations are similar to those noted in collagen in sections of other connective tissues.[14,18] Fibrils 500 Å in diameter have been seen quite close to osteoblasts and *unassociated with* very narrow ones, which suggests that the fibrils in newly forming osteoid normally are built up rapidly without any appreciable fine fibril stage. In the narrow zone of uncalcified osteoid which normally lies between the cell surface and the calcified osteoid, the collagen fibrils sometimes appear to be more widely separated than they are in the calcified osteoid (Fig. 10). In this small zone the fibrils may come closer together exactly at the moment of calcification or in the short period immediately after initial calcification.

One observes only the static situation in the micrograph, and the difference in organization in the fibrils from time to time could conceivably be the result of varying activity on the part of the osteoblast. Those fibrils which have been noted close together may have been formed in that fashion originally.

It has been shown previously in the rib of a 2-day-old child[21] that the fibrils may be rather loosely arranged even following calcification in some regions, and in the femoral metaphysis they appear in some places to be more loosely arranged than in others. The zone near the cell and extending into the calcified tissue is probably a chemically unstable one, and it seems likely that rearrangements occur here routinely in both the inorganic crystals and the organic collagen.

The number of cross striations visible in a "major period" in collagen fibers has been noted to decrease with age in bone in the same way as in other connective tissues (Fig. 9). The several striations often found by routine staining methods in each major period in newly formed bone are not nearly so evident, the technic being the same, in bone which has been established for some time.[24]

It also appears that the fibrils may become larger in diameter and slightly less dense in long-established bone. Fibrils of about 600 to 800 A have been observed in subperiosteal bone in the outer rib cortex of a middle-aged adult, while in bone from the same region of a senile adult fibril diameters of 1,000 and 1,500 A have been seen.[23]

Huber and Rouiller[12] described fibrils with diameters of 600 to 1,500 A in the cortex of the femoral and tibial diaphysis of 52- and 63-year-old adults. These measurements differ from those of Schwarz and Pahlke,[26] who used various bones and found that the most commonly occurring fibrils in old age were only about 600 A in diameter. They observed a slight increase in the thickness of the fibrils in bones of young children as compared with those of the embryo. In general, the fibril diameter reported by the latter authors are less than those reported by the other investigators for all ages, but in any event both Schwarz & Pahlke and Robinson & Watson noted a tendency for larger-diameter fibrils to be found in bone of specimens of comparable location from older subjects.

Fibril diameter and degree of fibril packing in different bone specimens vary. They may increase as bone in a given region matures, but also they may vary in different regions of the skeleton of the same subject.[9] Perhaps they vary in different animals. However, according to investigations so far reported, fibril diameter is never so small and fibril packing so loose in human bone that bone matrix appears like the epiphyseal cartilage matrix which the authors have investigated.

CALCIFICATION OF BONE MATRIX

In bone the initial calcification appears throughout the matrix shortly after it is formed, whereas in cartilage matrix it appears in separate foci over a comparatively wide area some time after matrix formation. Near the osteoblast, sometimes within 500 A of its surface, a few crystals or a small cluster of them appears in relation to a fibril. Close to this first evidence of calcification, the "normal" osteoid becomes filled with a mass of crystals. The first crystals lie with their long axis more or less parallel to the long axis of the fibrils, but, although calcification starts in close association with the fibril surface, the exact relation of the first crystals to specific prosthetic groups on the polypeptide chains in the collagen fibril is not known. The point as to whether calcification occurs inside the fibril as well as on the surface of the fibril is open to some argument.[24,27] Electron micrographs supporting both views may be shown. Perhaps some fibrils calcify internally and others do not.

The very earliest calcification in embryonic bone is reported by Jackson and Randall.[13] Now that more is known about the chemistry of collagen and the spatial relationships of its structural units, this observation may help investigators to pinpoint that chemical unit in collagen of calcifying matrices which is primarily involved in the inception of the calcification process. However, in the electron micrograph that they published, the crystals of apatite apparently



FIG. 11. Electron micrograph of material similar to that in Figure 10. The uncalcified osteoid is seen at one edge (B). *The fibrils of collagen appear more closely* packed in this instance than those in Figure 10. Their direction can be observed, although the fibrils are less clearly resolved than are those in the micrographs in Figure 9. At the "calcification front" one observes the sudden transition from uncalcified osteoid to heavily calcified osteoid. In the very periphery of the calcification (*B*) the long axis of the larger crystals generally parallels the fibril direction. However, it is (C) a little farther from the ossification front that one observes the pattern so typical of human bone wherein the long crystal axis closely parallels the long axis of the associated collagen fibril, and there is a concentration of crystals about every 630 A along the long collagen axis which duplicates the major period of the collagen.

lie between the *d and the a-b regions* of the fibrils in most instances, although inorganic densities appear occasionally to lie adjacent to other regions of the fibrils Robinson and Watson concluded that in newly formed bone the inorganic material was definitely observed in conjunction with collagen fibrils in conjunction with the dense bands of the fibrils, and more specifically that it may first appear *in relation* to any of the 5 minor bands (a, b, c, d and e) in each major collagen period.[24]

Shortly after the osteoid first becomes mineralized the crystals seem to change their relationship to the fibrils, inasmuch as they appear *concentrated* at the major band areas *(Fig. 11): the region of the a, b, b¹ and* c minor bands in each major period. Their average length also appears to decrease slightly.[24] In this same zone, where apparently there is regrouping of crystals with the fibrils, the fibrils also appear to be rearranged into a more regular pattern, one in which they are not only more closely packed than in the uncalcified osteoid zone next to the cell but also aligned so that their band areas are in register (Fig. 9).

As the degree of mineralization increases, the calcified bone matrix takes on an appearance which is very different from that of the calcified cartilage. There are areas of crystal-fiber orientation in bone and no areas of exactly the same crystal orientation in the fully calcified epiphyseal cartilage matrix *(Figs. 8 & 11)*.

SOME GENERAL REMARKS ABOUT THE STRUCTURE *OF CARTILAGE AND BONE*

The organic matrix of bone is organized differently from that of epiphyseal cartilage. *Of course, the collagen fibril and the muco*polysaccharide cement-substance components may be the same or chemically quite similar in cartilage and bone. Obviously, bone matrix contains less cement substance and more collagen per unit volume than does epiphyseal cartilage matrix. Investigations suggest that the mucopolysaccharides are generally more hydroscopic than collagen.[2,25] A large water content and a disperse fibril arrangement would give cartilage specific characteristics as a skeletal structure when uncalcified, among which would be elasticity, flexibility and an ability to dis-

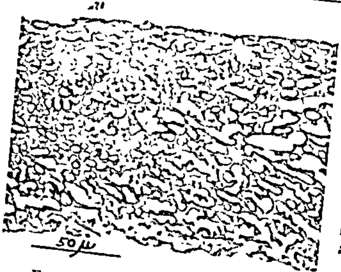


FIG. 12. Cross section, full thickness, cortex of diaphysis of the femur of a new-born puppy. Note the large marrow-vascular space distributed between the calcifiable osteoid matrix, or true bone tissue, of the whole bone specimen. The specific gravity of this specimen when hydrated was 1.42.



FIG. 13. Cross section, full thickness, cortex of diaphysis of femur of an 8-week-old puppy. Note that less of the total volume of this whole bone specimen is marrow-vascular space (compared with Fig. 12) and more is true bone tissue, or calcifiable osteoid. The specific gravity of this specimen when hydrated was 1.85.

tribute a load quickly over a large part of any joint surface that it might cover.

Calcified epiphyseal cartilage per unit volume can contain more calcium phosphate than bone[10] and, when fully calcified, appears more dense than bone, particularly in microradiographs. Epiphyseal cartilage matrix and bone matrix do not appear to expand during calcification. The present supposition is that in bone and cartilage, as in enamel,[6] the inorganic crystals may replace water.[22] This displaceable water is probably that which resides in the cement substance in the uncalcified state of bone and cartilage matrix. Thus, in equal volumes of bone and epiphyseal cartilage matrix, more room for crystal deposition would exist in epiphyseal cartilage matrix. On the other hand, more space in bone matrix would be occupied by collagen, and other dry organic components, than in epiphyseal cartilage matrix. This theory does not contradict the observation that the first crystals in bone and cartilage form at a collagen cement substance interface, or that the collagen fibrils are somehow instrumental in concentrating phosphorus or calcium, or both, at the crystal-inception points. It only suggests that once calcification starts at a point along a collagen fibril, the crystals actually form in the cement substance, replacing the water originally hydrating the cement substance. Furthermore, it does not contradict the concept that the fibrils may orient the adjacent mucopolysaccharide molecules, so that crystals formed in such oriented cement substance are oriented secondarily to the fibrils, as in bone.[24] Thus, where the fibrils are larger and more numerous, as in bone, there will be less room for crystals, but the crystals may be more clearly oriented to the fiber axis; whereas, where the fibrils are smaller and less numerous, as in epiphyseal cartilage, there will be more room per unit volume for crystals, but a large number of the crystals may not be oriented to the fibrils.

Recent studies tend to show that in *normal* animals of all ages, except for very small differences in *over-all* calcification in a bone specimen,[1] the calcified osteoid, or in other words the actual bone tissue in a normal whole bone, is very similar in organic and inorganic composition. Therefore, it is interesting to compare full-thickness cross



FIG. 14. Cross section, full thickness, cortex of diaphysis of femur of an adult dog. As the marrow-vascular space increased in relation to the calcifiable osteoid in the whole bone specimen, the specific gravity when the bone was hydrated had risen to 2.05.

sections of the diaphysis of femurs of three dogs: a newborn puppy, a puppy about 2 months old and an adult dog. The density of the three diaphyseal specimens, when hydrated and after they were stripped of periosteum and available marrow, varied widely: 2.05, 1 85 and 1.42, respectively.[21,22] The three sections in Figures 12, 13 and 14 came from these three samples, and each was considered to be representative of its sample. The density of the same specimens when dry were all 2.33 ± 0.03. Obviously the physical characteristics of a *whole* bone such as a femur will vary widely, depending on the way the calcified osteoid is spatially organized in it. Even though in a whole bone the actual calcified osteoid per unit of normal *osteoid* volume varies insignificantly on chemical and physical analysis, the whole bone, including the marrow and the periosteum, in which the normal osteoid resides may have very different chemical and physical analysis patterns, depending on the way the calcified normal osteoid is distributed in it In a large measure the ability of a bone to resist breaking forces will also depend on this microscopic pattern of organization.

REFERENCES

1. Amprino, R., and Engström, A.: Studies on x-ray absorption and diffraction of bone tissue, Acta anat. 15:1-22, 1952.
2. Blumberg, B. S., and Oster, G.: Light scattering studies on hyaluronic acid, Science 120:432-433, 1954.
3. Brandenburger, E., and Schinz, H. R.: Über die Natur der Verkalkungen bei Mensch und Tier und das Verhalten der anorganischen Knochensubstanz im Falle der hauptsächlichen menschlichen Knochenkrankheiten, Helvet. med. acta 12: 1-63 (Supp. 16) 1945.
4. Brower, T. D.: The localization of chloride in hyaline cartilage by histochemical technique, J. Bone & Joint. Surg. 38A:655-659, 1956.
5. Cameron, D. A., and Robinson, R. A.: [illegible] id ar- [illegible] of the [illegible]
6. Deakins, M.: Changes in the ash, water and organic content of pig enamel during calcification, J. Dent. Res. 21:429-435, 1942.
7. DiStefano, V., Neuman, W. F., and Rouser, G.: The isolation of a phosphate ester from calcifiable cartilage, Arch. Biochem. 47:218-220, 1953.
8. Eichelberger, L., Brower, T. D., and Roma, M.: Histochemical characterization of inorganic constituents, connective tissue, and the chondroitin sulphate of extracellular and intracellular compartments of hyaline cartilage, Am. J. Physiol. 166:328-339, 1951.
9. Frank, R., Frank, P., Klein, M., and Fontaine, R.. L'os compact humain normal au microscope électronique, Arch. anat. Microscop. 44:191-206, 1955.
10. Gaillard, P. J (Prof.). In vitro studies of the action of parathyroid products on mouse skull bone in tissue culture (a time-lapse movie). Presented by Professor Gaillard at The Johns Hopkins Hospital on October 1, 1956, in a lecture sponsored by the Finney-Howell Cancer Research Laboratory. Investigation conducted at the Laboratorium voor Cytologie en Experimentale Histologie der Rijksuniversiteit, Leiden, Holland.
11. Ham, A. W.: Some histophysiological problems peculiar to calcified tissues, J. Bone & Joint Surg. 31A:701-728, 1952
12. Huber, L., and Rouiller, Ch.: Les fibrilles collagènes de l'os. Experentia 7:338, 1951.

13. Jackson, S. F., and Randall, J. T.: The fine structure of bone, Nature 178:789, 1956.
14. Martin, A. V. W.: Electron microscope studies of collagenous fibers in bone, Biochim. et Biophys. acta. 10:42-48, 1953.
15. Neuman, W. F., and Neuman, M. W.: The nature of the mineral phase of bone, Chem. Rev. 53:1-45, 1953.
16. Owen, M., Jowsey, J., and Vaughan, J.: Investigation of the growth and structure of the tibia of the rabbit by microradiographic and autoradiographic techniques, J. Bone & Joint Surg. 37B:324-342, 1955.
17. Partridge, S. M.: The chemistry of connective tissues: I. The state of combination of chondroitin sulphate in cartilage, Biochem. J. 43:387-397, 1948.
18. Randall, J. T., Fraser, R. D. B., Jackson, S. F., Martin, A. V. W., and North, A. C. T:. Aspects of collagen structure, Nature 69:1029-1033, 1952.
19. Robinson, R. A.: An electron microscopic study of the crystalline inorganic component of bone and its relationship to the organic matrix, J. Bone & Joint Surg 31A: 389-435, 1952.
20. Robinson R. A., and Cameron, D A.: Electron microscopy of cartilage and bone matrix at the distal epiphyseal line of the femur in the newborn infant, J. Biophysic. & Biochem. Cytol. 2:253-260 (Supp.) 1956.
21. Robinson, R. A., and Elliott, S. R., 3rd: The water content of bone. I. The mass of water, inorganic crystals, organic matrix and "CO_2 space" components in an unit volume of dog bone, J. Bone & Joint Surg. 39-A:167-188, 1957.
22. ———: The water content of bone: II. The distribution of water among the various components of dog bone. (Unpublished work)
23. Robinson, R. A., and Watson, M. L.: Collagen-crystal relationships in bone as seen in the electron microscope, Anat. Rec. 114: 383-410, 1952.
24. ———: Crystal-collagen relationships in bone as observed in the electron microscope: III. Crystal and collagen morphology as a function of age, Ann. New York Acad. Sc. 60:596-628, 1955.
25. Rougvie, M. A., and Bear, R. S.: An x-ray diffraction investigation of the swelling of collagen, J. Am. Leather Chem. Assoc. 48:735-751, 1953.
26. Schwarz, W., and Pahlke, G.: Elektronemikroskopische Untersuchungen an der Interzellularsubstanz des menschlichen Knochengewebes, Ztschr. Zellforsch. u. mikr. Anat. 38:475-487, 1953.
27. Watson, M. L., and Avery, J. K.: The development of the hamster lower incisor as observed by electron microscopy, Am. J. Anat. 95:109-162, 1954.
28. Watson, M. L., and Robinson, R. A.: Collagen crystal relationships in bone as seen in the electron microscope: II. Electron microscopic study of basic calcium phosphate crystals, Am. J. Anat. 93:25-60, 1953.
29. Zbinden, G.: Ueber Feinstruktur und Alters-veränderungen des hyalinen Knorpels in elektronmikroskopischen Schnittpräparat und Beitrag zur Kenntnis der Verfettung der Knorpelgrundsubstanz, Schweiz. Ztschr. allg. Path. 16:165-189, 1953.

Le Matrice Organic de Osso e Cartilagine Epiphysee

Summario in Interlingua

Es signalate le differentia structural inter differente matrices de cartilagine e etiam le differentia structural inter matrices de cartilagine e de osso Es usate non solmente le datos obtenite per le proprie investigationes del autores sed etiam le datos obtenite per alteres. In iste typo de revista de matrices organic de histos conjunctive que es normalmente destinate a calcificar se, il non es possibile proceder sin discuter etiam le processo calcificatori. Iste processo es prendite in consideration in conjunction con micrographias electronic de noncalcificate e discalcificate matrices de cartilagine epiphysee e de osso. Finalmente, le structura de cartilagine e de osso es ponite in correlation general con le characteristicas structural de iste histos.

4

Definitions, Terminology and Classification of Metabolic Bone Disorders

EDWARD C. REIFENSTEIN, JR., M.D.*

DEFINITIONS AND TERMINOLOGY

METABOLIC BONE DISORDERS

Definition. Generalized or systemic diseases by definition influence all tissues of the human body, including bone. The osseous lesions that result from such disturbances are classified as metabolic bone disorders (Fig. 1 B).

Problems in Differentiating Metabolic Bone Disorders. Skeletal pathology arising from generalized disease is much more common than is apparent from a compilation of the number of cases currently diagnosed as having metabolic bone disorders. This discrepancy largely is the result of difficulty in diagnosing two groups of cases: those with early stages or mild states of generalized bone *involvement, those with both systemic* and localized osseous manifestations.

EARLY STAGES OR MILD STATES. The skeletal involvement in the early stages or in the mild states of systemic disease is not detectable by the technics currently available to clinicians for studying the bones of the human during life.

EXAMPLES OF PRESENCE OF BONE INVOLVEMENT BEFORE IT NOW CAN BE DETECTED. Osteoporosis associated with the menopausal state begins to develop as soon as the hormonal alterations of the menopause *are well established; however, the* disease is not recognizable for several years by the current clinical or laboratory procedures. Similarly, the osseous involvement that sometimes arises from alterations in the calcium homeostasis of the body fluids is initiated as soon as the changes in calcium regulation occur; again, the bone lesions are not detectable with the current technics until the disordered mineral metabolism has been *present for months to years.*

EXAMPLES OF LIMITATIONS IN CURRENT TECHNICS FOR STUDYING BONE IN LIVING MAN. *Roentgenograms.* The early states of bone disease involving too little calcified bone escape recognition in roentgenograms because it is impossible by visual examination to detect with accuracy changes in density until at least 30 per cent of the calcium content has been lost. Similarly, it is very *difficult to detect recalcification by x-ray,* because a considerable amount of calcium must be regained before an increase in density can be recognized in the films.

Serum Chemical Determinations. An abnormality in the concentration of a mineral constituent of the body fluids often does not indicate an abnormal status of that mineral as a component of calcified bone; an example is the hypercalcemia of *hyperparathyroidism* without bone involvement. On the other hand, a normal mineral concentration

* From the Medical Division, The Squibb Institute for Medical Research, E. R. Squibb & Sons Division, Olin Mathieson Chemical Corporation, New York, and the Department of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals, New York, N. Y.

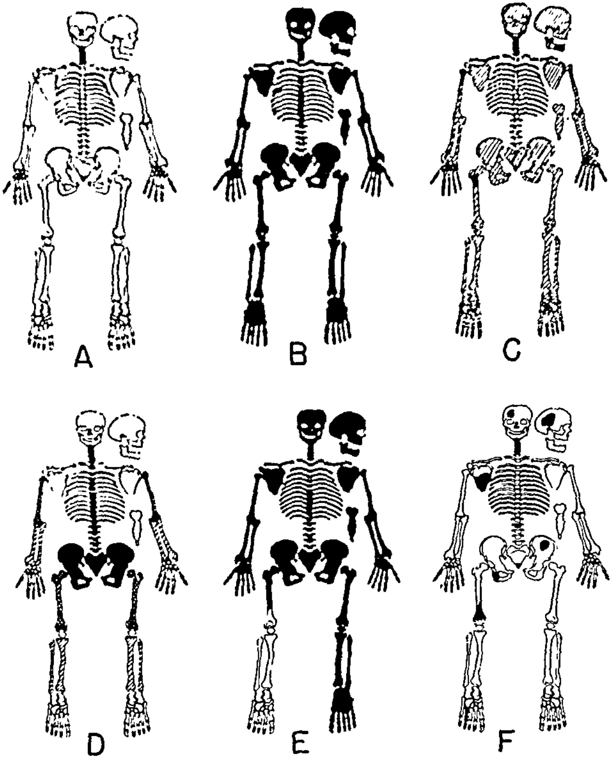


FIG. 1. Illustrating "Generalized" and "Localized" bone disorders as defined by the author. A black area represents marked bone disease; a shaded area, mild bone disease; a white area, no bone disease (normal bone). (A) Normal skeleton. (B) Skeleton with generalized bone disease. (C) Skeleton with the generalized bone disease, *osteitis fibrosa generalisata*, complicating hyperparathyroidism, showing localized osseous lesions and generalized bone involvement. (D) Skeleton with the generalized bone disease, *osteoporosis*, showing an orderly predilection for the greatest involvement in the spine and the pelvis, for moderate involvement in the long bones, and for the least involvement in the skull and certain other bones. (E) Skeleton with the localized bone disease, Paget's disease of bone, showing extensive but not generalized involvement. (F) Skeleton with the localized bone disease, polyostotic fibrous dysplasia, showing widely disseminated individual lesions without generalized bone involvement. (*Modified from* Albright & Reifenstein: The Parathyroid Glands and Metabolic Bone Disease: Selected Studies, Baltimore, Williams & Wilkins)

4

Definitions, Terminology and Classification of Metabolic Bone Disorders

EDWARD C. REIFENSTEIN, JR., M.D.*

DEFINITIONS AND TERMINOLOGY

METABOLIC BONE DISORDERS

Definition. Generalized or systemic diseases by definition influence all tissues of the human body, including bone. The osseous lesions that result from such disturbances are classified as metabolic bone disorders (Fig. 1 B).

Problems in Differentiating Metabolic Bone Disorders. Skeletal pathology arising from generalized disease is much more common than is apparent from a compilation of the number of cases currently diagnosed as having metabolic bone disorders. This discrepancy largely is the result of difficulty in diagnosing two groups of cases: those with early stages or mild states of generalized bone involvement; those with both systemic and localized osseous manifestations.

EARLY STAGES OR MILD STATES. The skeletal involvement in the early stages or in the mild states of systemic disease is not detectable by the technics currently available to clinicians for studying the bones of the human during life

EXAMPLES OF PRESENCE OF BONE INVOLVEMENT BEFORE IT NOW CAN BE DETECTED. Osteoporosis associated with the menopausal state begins to develop as soon as the hormonal alterations of the menopause are well established; however, the disease is not recognizable for several years by the current clinical or laboratory procedures. Similarly, the osseous involvement that sometimes arises from alterations in the calcium homeostasis of the body fluids is initiated as soon as the changes in calcium regulation occur; again, the bone lesions are not detectable with the current technics until the disordered mineral metabolism has been present for months to years.

EXAMPLES OF LIMITATIONS IN CURRENT TECHNICS FOR STUDYING BONE IN LIVING MAN. *Roentgenograms.* The early states of bone disease involving too little calcified bone escape recognition in roentgenograms because it is impossible by visual examination to detect with accuracy changes in density until at least 30 per cent of the calcium content has been lost. Similarly, it is very difficult to detect recalcification by x-ray, because a considerable amount of calcium must be regained before an increase in density can be recognized in the films.

Serum Chemical Determinations. An abnormality in the concentration of a mineral constituent of the body fluids often does not indicate an abnormal status of that mineral as a component of calcified bone; an example is the *hypercalcemia of hyperparathyroidism* without bone involvement. On the other hand, a normal mineral concentration

* From the Medical Division, The Squibb Institute for Medical Research, E. R. Squibb & Sons Division, Olin Mathieson Chemical Corporation, New York, and the Department of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals, New York, N. Y.

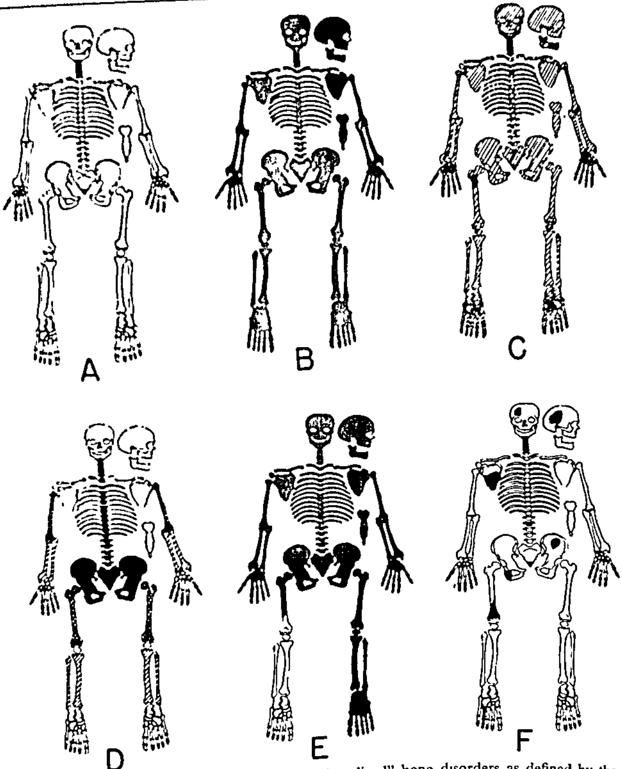


FIG. 1. Illustrating "Generalized" and "Localized" bone disorders as defined by the author. A black area represents r ... shaded area, mild bone d... a white area, no bone disease (... with generalized bone disease. ((... fibrosa generalisata, complicating ... and generalized bone involvement ... porosis, showing an orderly prec ... the pelvis, for moderate involvement in the leg ... involvement in the skull and certain other bones. (E) Skeleton with the localized bone disease, Paget's disease of bone, showing extensive but not generalized involvement. (F) Skeleton with the localized bone disease, polyostotic fibrous dysplasia, showing widely disseminated individual lesions without generalized bone involvement. (Modified from Albright & Reifenstein: The Parathyroid Glands and Metabolic Bone Disease: Studies, Baltimore, Williams & Wilkins)

in the body fluids can occur in the presence of marked bone involvement; an example is the normocalcemia of postmenopausal osteoporosis.

Bone Biopsy Specimens. The various parts of the skeleton differ markedly in anatomic structure, chemical composition and responsiveness to physiologic and pathologic influences; therefore, pieces of bone obtained by biopsy are not representative samples of the entire skeletal mass or even of the diseased portion of it. The data obtained from chemical analysis of an individual bone sample may give no indication of marked changes that have taken place in the total mass of calcified tissue in the whole bone from which the specimen was obtained, or in the total mass of other portions of the skeleton. Furthermore, bone specimens often fail to exhibit abnormalities histologically until chemical disturbances have been present for a long time.

Metabolic Balance Studies. The technics for measuring in man the total mineral and nitrogen balances are sufficiently precise and sensitive to detect only the gross disturbances in the physiologic equilibrium between the intake and the output of minerals in the skeleton, and are of no assistance in obtaining a quantitative measure of the total mass of calcified bone.

SYSTEMIC DISORDERS WITH LOCALIZED LESIONS. The generalized nature of the bone involvement often is overlooked because attention is focused on the localized osseous lesions, since it is not uncommon for some parts of the skeleton to respond with a more pronounced degree of the metabolic bone disorder than others.

EXAMPLES OF GENERALIZED OSSEOUS DISORDERS MASKED BY LOCALIZED LESIONS. As a manifestation of the bone disease (osteitis fibrosa generalisata) that complicates hyperparathyroidism, there may be localized cysts and tumors that catch the eye, while the generalized decalcification is missed (Fig. 1 C). Conversely, the generalized nature of the bone disorder may be questioned because certain bones fail to respond. For example, although all tissues of the body (including the bones) are affected by estrogen deficiency, the skull usually is not involved detectably, even when the vertebrae, the pelvis and the long bones show marked evidence of osteoporosis (Fig. 1 D). Similarly, the generalized atrophy (osteoporosis) of disuse of a patient immobilized in bed does not involve the skull and the mandibles, since these bones are used as much when the patient is in bed as when he is up and about.

LOCALIZED BONE DISORDERS

Definition. The one point that is essential in establishing that a bone disorder is localized is the demonstration of an uninvolved area of normal bone. In most cases this presents no problem.

Problems in Differentiating Localized Bone Disorders. In certain circumstances the differentiation between a localized and a systemic bone disorder may be difficult. *The problem arises in diagnosing two* groups of cases: those with extensive or disseminated localized osseous lesions; those with metabolic osseous disturbances superimposed upon localized bone lesions.

WIDESPREAD LOCALIZED BONE LESIONS. The localized bone disease may be so extensive or disseminated that initially it appears to be a systemic disorder.

EXAMPLES OF WIDESPREAD LOCALIZED LESIONS MISTAKEN FOR GENERALIZED OSSEOUS INVOLVEMENT. In Paget's disease of bone, 95 per cent of the skeleton may be involved, but, by a careful roentgenographic survey, normal bone (with a sharp line of demarcation between it and involved bone) can be found in some area (Fig. 1 E). In an occasional patient the osseous lesions of multiple myeloma may be very small and distributed so diffusely throughout the vertebrae (Kahler's disease) that the roentgenographic picture is mistaken for that observed in the metabolic bone disorders with too little calcified bone (osteoporosis, osteomalacia and osteitis fibrosa generalisata). In such cases the diagnosis of multiple myeloma may be established only after the patient has been

Table 1. Outline of Some Characteristic Features of Certain Specific Metabolic Bone Disease Entities and of Names to Designate Them

Characteristics of Specific Metabolic Bone Disease Entity	Normal Bone	Names Used to Designate Specific Metabolic Bone Disease Entities				
		Osteoporosis	*Osteomalacia*	*Osteitis Fibrosa Generalisata*	*Hyperosteogenesis*	*Osteosclerosis*
Total amount of calcified bone mass	Normal mass (Normomass)	Too little mass (Hypomass)	Too little mass (Hypomass)	Too little mass (Hypomass)	Too much mass (Hypermass)	Too much mass (Hypermass)
Total amount of calcified bone	Normal amount of calcified bone	Too little calcified bone	Too little calcified bone	Too little calcified bone	Too much calcified bone	Too much calcified bone
Appearance of roentgenographic image of calcified bone	Normal density (Normopaque) (Normolucent)	Too little density (Hypopaque) (Hyperlucent)	Too little density (Hypopaque) (Hyperlucent)	Too little density (Hypopaque) (Hyperlucent)	Too much density (Hyperpaque) (Hypolucent)	Too much density (Hyperpaque) (Hypolucent)
Relation of bone formation to bone resorption in primary stage	Dynamic equilibrium	Too little bone formation	Too little bone formation	Too much bone resorption	Too much bone formation	Too little bone resorption
Histologic appearance of bone in primary stage	Normal	Too little formation of matrix	Too much formation of matrix; too little calcification of matrix	Too much resorption of matrix and mineral	Too much formation of matrix; normal calcification of matrix	Too little resorption of matrix and mineral
Ratio of total amount of mineral to total amount of matrix	Normal	Normal	Reduced	Normal	Normal	Normal
Ratio of total amount of matrix in this disorder to that in normal bone	Normal	Reduced	Increased	Reduced	Increased	Increased
Ratio of total amount of mineral in this disorder to that in normal bone	Normal	Reduced	Reduced	Reduced	Increased	Increased

order have been modified by compensatory mechanisms as the bone condition progresses. Furthermore, pathologic terms should not be used to describe physiologic processes.

Examples of Compensatory Mechanisms Which Modify the Initial Metabolic Bone Disorders. The fundamental pathologic physiology of *osteoporosis* in the primary stage of the disease is too little formation of bone; eventually, however, as the mass of calcified bone decreases, the remaining bone becomes abnormally responsive to the physiologic stimulus of the stress and strain of weight-bearing, and the process of bone formation increases until the amount of bone formation is restored to that in normal bone. At this secondary stage, the patient still has too little bone mass and too little calcified bone, and still has the disease *osteoporosis,* even though the processes of bone formation and bone resorption have been restored to a dynamic equilibrium and the bone by histologic examination no longer shows a decrease in matrix formation. Such a bone is still an *osteoporotic* bone in the sense that it is present in a patient with *osteoporosis.* It is apparent that difficulty arises in describing this sequence of events if one uses the term *osteoporotic* as synonymous with an absence of matrix formation as observed in the microscopic section.

Another example is pertinent. An excessive amount of uncalcified matrix is properly described as a "wide osteoid seam." Wide osteoid seams occur not only in osteomalacia but also physiologically during normal rapid growth in children. If a bone with wide osteoid seams is referred to as an *osteomalacic* bone, one is faced with the paradox of using a pathologic term to describe a normal physiologic process. It appears logical to avoid terminology which would require every human being to have *osteomalacic* bone during the normal process of rapid growth.

Loss of Significance of Words Through Misuse. Certain words, such as *decalcified* and *demineralized,* which have been employed widely in the past to characterize the state of bone in certain metabolic bone disorders, have been misused so consistently without regard to their applicability to the actual osseous processes they attempt to describe that they have lost much of their useful significance as specific terms. For this reason, words such as these have been omitted deliberately from Table 1.

Examples of Misuse: "Decalcified" and Similar Words. One of the most abused words in the field of bone disorders is *decalcified.* Literally this word means "to have had the calcium removed" *Decalcified* is properly used to describe a bone section which has had the calcium removed to prepare it for histologic study. However, there is only one metabolic bone disorder—*osteitis fibrosa generalisata*—in which there seems to be any justification for using the word *decalcified,* and then only in a limited and an indirect connection. In living bone, increased bone resorption results in the removal from the calcified bone of both the calcium and the protein matrix. It has never been demonstrated convincingly in vivo that the calcium can be removed and the matrix left behind. Thus, in *osteitis fibrosa generalisata* there actually is no bone tissue that has been *decalcified,* but only a decreased mass of normal bone that as yet has not been resorbed. In relation to normal man, the patient with *osteitis fibrosa generalisata,* in a total quantitative sense, has been *decalcified* and likewise by the loss of bone matrix *deproteinized;* in the same sense, the total skeletal mass of calcium could be *decalcified* and *deproteinized* by amputating one limb.

But if, because of established usage, one accepts the word *decalcified* (or similarly *demineralized*) as describing the state of too little calcified bone as a result of excessive bone resorption, he cannot use this term to describe the state of bone in *osteomalacia.* In this latter condition there is a failure of calcium to be deposited in the matrix; therefore, this matrix properly can be described as *acalcified* or *uncalcified* (*amineralized* or

unmineralized). Finally, it should be obvious from the foregoing that the bones in *osteoporosis* are not *decalcified*. In a general sense they are *acalcified* in relation to the bones of the normal state, since the bones in *osteoporosis* fail to take up as much calcium as normal bones because of a lack of matrix into which the mineral can be deposited. Therefore, the bones in *osteoporosis* also are *aproteinized* in relation to those of the normal state. Strictly speaking, the bones in *osteoporosis* are *acalcified* because they have been *aproteinized*. Because of the difficulties in employing the terms precisely, the author avoids as much as possible the words *decalcified, demineralized, deproteinized, acalcified, amineralized* and *aproteinized*.

Lack of Diagnostic Help from Hypopacity and Deformity of Bone. It can be seen in Table 1 that in three different metabolic bone conditions *(osteoporosis, osteomalacia* and *osteitis fibrosa generalisata)* hypopaque bone is observed in the roentgenograms. It seems necessary to emphasize that it is impossible to determine which one of these metabolic bone disorders is present merely from the fact that too little density is present. Furthermore, it should be obvious that any bone which contains too little calcified mass may develop any structural deformity that results from insufficient bone strength. Again, it is not possible to differentiate among the three metabolic bone disturbances, since the same types of deformities have been observed in all three.

Examples of Same Types of Deformities Occurring in Different Bone Disorders. Deformities of the vertebrae (codfish vertebra, wedged vertebra, crushed vertebra, herniation of the nuclei pulposi into the end-plate of the vertebra) occur in *osteoporosis, osteomalacia* and *osteitis fibrosa generalisata*, although they may be somewhat more common in *osteoporosis*.

Diagnostic Assistance from Location of Osseous Lesions. While it is true that some difference in the structure of the bone in these three disorders with too little calcified bone *(osteoporosis, osteomalacia* and *osteitis fibrosa generalisata)* may be apparent in the roentgenographic image to those experienced in interpreting roentgenograms, greater assistance in predicting the nature of the metabolic bone disorder can be derived from the location of the osseous lesions and from other associated manifestations.

Examples of Diagnostic Assistance Derived from Location of Osseous Lesions. *Osteoporosis* commonly involves the spine, the pelvis and the long bones, but rarely the skull and the extremities; *osteomalacia* frequently involves the extremities; *osteitis fibrosa generalisata* frequently involves the skull. Furthermore, the degree of involvement usually is greater in *osteitis fibrosa generalisata* and leads more often to an absence of the lamina dura. The occurrence of bone cysts and of *brown tumors* in *osteitis fibrosa generalisata* and of pseudofractures in *osteomalacia* is of considerable diagnostic assistance. There is a greater tendency for the bones to bend in *osteomalacia*, while spontaneous fractures are more prone to occur in *osteoporosis* and in *osteitis fibrosa generalisata*.

Nonspecificity of Roentgenographic Findings. From the previous discussion it is apparent that the most careful interpretation that can be made of the evidence in the roentgenographic films of bones with generalized hypopacity usually will fail to establish the exact nature of the specific metabolic bone disorder that is present, although it may suggest the most likely diagnosis. Hence, in patients with osseous disturbances characterized by too little calcified bone, the roentgenographic findings should be reported in a manner which indicates that a metabolic bone disorder of undetermined nature is present and suggests that one of the specific disease entities is the most likely candidate for the diagnosis.

Example of a Roentgenographic Report in Metabolic Bone Disorders with Too Little Calcified Bone. A report on the roentgenographic findings in a patient with a metabolic bone disorder characterized

by too little calcified bone might be phrased as follows: "The films reveal generalized hypopacity of the bones, probably indicating the presence of a metabolic bone disorder of undetermined nature. The distribution of the involvement and the occurrence of certain lesions (such as cysts or pseudofractures) and of other associated manifestations (such as the absence of the lamina dura or the presence of bending or fractures) are most consistent with a diagnosis of the metabolic bone disorder *(osteoporosis, osteomalacia* or *osteitis fibrosa generalisata)* rather than of one of the other osseous disturbances associated with hypopaque bone."

CLASSIFICATION OF METABOLIC BONE DISORDERS

AUTHOR'S CLASSIFICATION

The considerations upon which the author's classification of metabolic bone disorder is based have been discussed in detail elsewhere.[9] Except for modifications in minor details, the classification is essentially that given in 1948 by Albright and Reifenstein.[1]

Classification in Terms of the Mass of Calcified Bone and the Status of the Bone-Forming and the Bone-Resorbing Processes. The metabolic disorders of bone can be divided into two main groups in terms of the total amount of calcified bone that is present in the body; there can be either *too little* or *too much* calcified bone. In a healthy adult the total mass of calcified bone in the body is in a state of dynamic equilibrium with the net gain from the process of bone formation equal to the net loss from the process of bone resorption. Therefore, an alteration in the total amount of calcified bone can be brought about in two ways—by changing either the amount of bone formation or the amount of bone resorption. Metabolic bone disorders are classified according to this scheme in Table 2.

TABLE 2. CLASSIFICATION OF METABOLIC BONE DISORDERS

Too little calcified bone
- Bone formation too little
  - Too little formation of matrix: Osteoporosis
  - Too little calcification of matrix: Osteomalacia or rickets
- Bone resorption too much
  - Too much resorption of matrix and calcium: Osteitis fibrosa generalisata

Too much calcified bone
- Bone formation too much
  - Too much formation of matrix: Hyperosteogenesis
  - Too much calcification of matrix: Nonexistent
- Bone resorption too little
  - Too little resorption of matrix and calcium: Osteosclerosis

DETAILS OF CLASSIFICATION. It will be noted in Table 2 that further subdivision is necessary, since bone formation consists of two steps: (1) the laying down of the matrix by the osteoblasts; and (2) the deposition of the calcium salts into this matrix. Thus, there may be a deficiency in the *formation of the matrix* or a deficiency in the *calcification of the matrix,* either of which can lead to too little bone formation. When the defect is in matrix formation, the specific metabolic bone disorder that results is spoken of as *osteoporosis,* when the defect is in calcification of the matrix, the specific metabolic bone disorder is spoken of as *osteomalacia* (adult rickets). Also, too little calcified bone may be the result of too much bone resorption, which produces the metabolic bone disease called *osteitis fibrosa generalisata.* Too much calcified bone occurs either from too much bone formation or too little bone resorption. Too much bone formation arises from increased matrix formation; this condition is listed in Table 2 as *hyperosteogenesis.* However, too much bone formation because of excessive calcification of the matrix does not occur, since it appears that matrix either *is* or *is not* calcified and cannot be *supercalcified.* Hence, in Table 2 there is no disorder under the heading "Too

Much Calcified Bone" which corresponds to *osteomalacia* under the heading "Too Little Calcified Bone." Too much calcified bone results also from too little bone resorption; the metabolic bone disorder is called *osteosclerosis.*

Advantages of Proposed Classification. The classification in Table 2 is useful from a clinical point of view, since it enables the physician to consider metabolic bone disturbances in terms that correlate with the impressions he has received from viewing the bones in roentgenograms. Furthermore, the classification forms a helpful basis for diagnostic and therapeutic considerations, since it includes as secondary divisions the several different causative mechanisms that lead to the same net change in the amount of calcified bone.

Definition of Terms: Osteoporosis. *Osteoporosis* is that category of too little calcified bone in which there is too little formation of bone because of insufficient formation of matrix. The total mass of calcified bone becomes reduced because the formation of bone is decreased while the resorption of bone continues at a normal rate. Some of the factors that seem to have a causal relationship to *osteoporosis* may be classified provisionally according to the scheme given in Table 3.

TABLE 3. PROVISIONAL CLASSIFICATION OF CAUSES OF OSTEOPOROSIS

Defect in osteoblasts
Loss of stress and strain
Atrophy (osteoporosis) of disuse
Deficient estrogen
Postmenopausal state
Premenopausal ovarian insufficiency
Congenital osteoplastic defect
Osteogenesis imperfecta
Defect in matrix
Deficient androgen
Senile state in males
Presenile testicular insufficiency
Deficient protein
Malnutrition
Avitaminosis C (scurvy)
Hyperthyroidism
Diabetes mellitus
Cushing's syndrome
Chronic corticoid therapy
Prolonged stress
Defect unknown
Acromegaly
Idiopathic osteoporosis

DISCUSSION OF CAUSES OF OSTEOPOROSIS. The activity of the osteoblasts must be normal for the formation of matrix to be adequate. Since the normal stimulus to the osteoblasts is the stress and strain of weight-bearing, loss of this stimulus results in osteoporosis of disuse. Adequate amounts of estrogen, androgen, protein substances, ascorbic acid and similar materials are needed for physiologic function of the osteoblasts; hence, a deficiency in any one of these factors results in a decrease in osteoblastic activity and, thus, in osteoporosis. Corticoid hormones favor the conversion of protein into energy, and, when continuously present in excess (as in Cushing's syndrome, chronic corticoid therapy or prolonged stress), they may interfere with matrix formation by creating a shortage of protein *building blocks,* thus producing osteoporosis. Hyperthyroidism and diabetes mellitus likewise may induce osteoporosis by diverting protein materials from matrix formation to energy production. The mechanism of the disturbance in acromegaly is not known, although it may be related either to the excess of pituitary hormones or to the associated deficiency in gonadal hormones. A bone disorder, which appears to be very similar to osteoporosis, occurs when the osteoblasts are congenitally defective, as in osteogenesis imperfecta. Finally, even when all the above causative factors have been eliminated, there are cases in which the etiology of the bone disorder is completely obscure; the bone disorder in this instance is termed *idiopathic osteoporosis.*

Definition of Terms: Osteomalacia. *Osteomalacia* is that category of too little calcified bone in which there is too little

TABLE 4. PROVISIONAL CLASSIFICATION OF CAUSES OF OSTEOMALACIA OR RICKETS

Insufficient absorption
- Low calcium absorption
  - Low calcium diet
  - Gastro-intestinal disease
  - Hyperthyroidism ?
- Low vitamin D absorption
  - Low vitamin D diet (*avitaminosis D*)
  - Gastro-intestinal disease
  - Hyperthyroidism ?
  - Vitamin D resistant rickets

Excessive excretion of calcium
- Loss from kidney
  - Calcium as a base in acidosis
    - Pyelonephritis with distal tubular damage
    - Fanconi syndrome with proximal tubular damage
  - Low renal threshold
    - Idiopathic hypercalcuria ?
    - Renal infection ?
  - Hyperthyroidism ?
- Loss from placenta
  - Frequent pregnancy
- Loss from breast
  - Prolonged lactation

Excessive utilization of calcium
- Bone formation too great
  - Healing osteitis fibrosa generalisata

Insufficient mobilization of calcium
- Bone resorption too little
  - Osteopetrosis with insufficient calcium intake

formation of bone because of insufficient calcification of matrix. The total mass of calcified bone becomes reduced because the formation of bone is decreased while the resorption of bone continues at a normal rate Some of the factors that seem to have a causal relationship to *osteomalacia* may be classified provisionally according to the scheme given in Table 4.

DISCUSSION OF CAUSES OF OSTEOMALACIA. The saturation of calcium and phosphorus cannot be reduced below the normal range if calcification of the matrix is to continue at a normal rate Decreased saturation may result from one or a combination of four factors: (1) insufficient absorption (when the diet is low in calcium or vitamin D, the gastro-intestinal tract is diseased, so that proper amounts of calcium or vitamin D *are not absorbed, or the calcium requirement* and the rate of calcium transport in the gastro-intestinal tract are greater than normal as a result of *increased thyroid activity*); (2) excessive excretion (when there is renal disease with increased elimination of calcium as a fixed base, a low renal threshold for calcium, excessive thyroid activity, frequent pregnancy or prolonged lactation); (3) excessive utilization (when abnormal bone resorption has been eliminated and compensatory bone repair is still continuing at an accelerated rate); or (4) insufficient mobilization (when the intake of calcium is low and the process of calcium release from bone is congenitally defective, as in *osteopetrosis*).

Definition of Terms: Osteitis Fibrosa Generalisata. *Osteitis fibrosa generalisata* is that category of too little calcified bone in which there is too much resorption of bone. The total mass of calcified bone becomes reduced because the rate of bone formation does not accelerate sufficiently to offset the increased rate of bone resorption. Some of the factors that seem to have a causal relationship to *osteitis fibrosa generalisata* may *be classified provisionally according to the* scheme given in Table 5.

TABLE 5. PROVISIONAL CLASSIFICATION OF CAUSES OF OSTEITIS FIBROSA GENERALISATA

Excessive parathyroid hormone
- Primary hyperparathyroidism
- Secondary hyperparathyroidism

Excessive acids in body fluids (chronic systemic acidosis)
- Renal acidosis with decreased glomerular *function. renal osteitis fibrosa generalisata* ("renal rickets")
- Renal acidosis with normal glomerular function

Excessive rate of cellular metabolism
- Hyperthyroidism

Excessive osteoclastic activity
- Poisoning with chemicals

Discussion of Causes of Osteitis Fibrosa Generalisata. When the need for calcium in the body fluids is increased beyond the normal requirement, the additional calcium is obtained first from the quantity that is present each day in the gastro-intestinal tract. If this amount is not adequate to offset the demand, stored calcium is withdrawn from bone. The need for increased calcium in body fluids may result from excessive parathyroid or thyroid hormone activity, or from excessive use of calcium as a fixed base to counteract acidosis. Occasionally chemical irritants may accelerate the rate of osteoclastic activity.

Definition of Terms: Hyperosteogenesis. *Hyperosteogenesis* is that category of too much calcified bone in which there is too much formation of matrix. The total mass of calcified bone becomes increased because the formation of bone is greater than normal while the resorption of bone continues at a normal rate. Some of the factors that seem to have a causal relationship to *hyperosteogenesis* may be classified provisionally according to the scheme given in Table 6.

Discussion of Causes of Hyperosteogenesis. The rate of osteoblastic activity may be accelerated beyond the normal level by a greater than normal amount of physiologic stimulation with excessive exercise. The acceleration may occur also as a compensatory response when there is too little calcified bone, as in *osteitis fibrosa generalisata* or *osteomalacia*. When the cause of these latter conditions is eliminated, the increased rate of osteoblastic activity cannot be reduced immediately to the physiologic level of function, and *hyperosteogenesis* occurs until the dynamic equilibrium between bone resorption and bone formation is reestablished. Accelerated bone formation may take place also with chemical poisons which irritate the osteoblasts and thus increase their activity.

Table 6. Provisional Classification of Causes of Hyperosteogenesis

- Poisoning with chemicals
  - Chronic lead poisoning (plumbism)
  - Fluorine poisoning (fluorosis)
  - Elemental phosphorus poisoning
  - Chronic radium poisoning
- Excessive stress
- Overcompensatory bone repair
  - Healing osteitis fibrosa generalisata
  - Healing osteomalacia

Table 7. Provisional Classification of Causes of Osteosclerosis

- Insufficient parathyroid hormone
  - Hypoparathyroidism
  - Parathyroid hormone resistance: pseudohypoparathyroidism
- Congenital osteoblastic defect
  - Osteopetrosis

Definition of Terms: Osteosclerosis. *Osteosclerosis* is that category of too much calcified bone in which there is too little resorption of bone. The total mass of calcified bone becomes increased because the resportion of bone is decreased while the formation of bone continues at a normal or only moderately reduced rate. Some of the factors that seem to have a causal relationship to *osteosclerosis* may be classified provisionally according to the scheme given in Table 7.

Discussion of Causes of Osteosclerosis. The rate of bone resorption decreases when the osteoclasts are deprived of, or are resistant to, physiologic quantities of parathyroid hormone (as in *hypoparathyroidism* or *pseudohypoparathyroidism*). The osteoclasts also may be congenitally incapable of functioning normally (as in *osteopetrosis*).

Classification of Other Investigators

A brief discussion is indicated of the classifications of metabolic bone disorders that have been proposed by certain other investigators.

Classification of Follis. Follis[5,6] has presented a classification of metabolic bone

disorders based on the phases of the growth of bone. He employs three main headings: (1) Disturbances in Growth of Cartilage; (2) Disturbances in Osteogenic-Osteolytic Balance; and (3) Disturbances in Deposition of Inorganic Elements in Cartilage Matrix and/or Osteoid.

According to this classification, Disturbances in Growth of Cartilage may be the result of increased activity from hyperpituitarism or hyperthyroidism, or of decreased activity from inanition, hypopituitarism, hypothyroidism or achondroplasia.

Disturbances in Osteogenic-Osteolytic Balance are subdivided into four headings: (1) Decreased Osteoblastic Activity; (2) Increased Osteoblastic Activity; (3) Decreased Osteolytic Activity; and (4) Increased Osteolytic Activity. The causes of Decreased Osteoblastic Activity are listed by Follis as (1) lack of essential nutrients, particularly ascorbic acid; (2) hypopituitarism; (3) hypothyroidism; and (4) excessive adrenal cortical "S" hormone. The causes of Increased Osteoblastic Activity are given as (1) increased local activity and blood supply; (2) acromegaly; (3) androgenic stimulation (?); (4) hyperestrogenism (mouse); and (5) hypertrophic osteoarthropathy. As causes of decreased osteolytic activity Follis gives: Marble bone disease and hyperestrogenism (rat). The causes of Increased Osteolytic Activity are listed as (1) acute severe inanition; (2) disturbance in serum calcium and/or phosphorus (hyperparathyroidism, hypervitaminosis D, nephritis, acidosis); (3) Paget's disease of bone; and (4) hypervitaminosis A.

Under the third main heading of Disturbances in Deposition of Inorganic Elements in Cartilage Matrix and/or Osteoid Follis gives: Defective calcium and/or phosphorus (rickets, osteomalacia) and excessive lead, bismuth and strontium.

Discussion of Classification of Follis. The author has some comments concerning the subheadings under the second main division, Disturbances in Osteogenic-Osteolytic Balance. The first of these subheadings, *Decreased Osteoblastic Activity,* is essentially the same as that given by the author in Table 2 as "Too Little Formation of Matrix," the end-result of which is *osteoporosis;* the causes enumerated by Follis are listed by the author in Table 3 as causes of *osteoporosis.* However, Follis does not include here as causes, loss of stress and strain, hypoestrogenism and hypoandrogenism, all of which are followed by *osteoporosis* in man.

The second subheading of Follis, *Increased Osteoblastic Activity,* resembles that given by the author in Table 2 as "Too Much Formation of Matrix," the end-result of which he calls *hyperosteogenesis.* In regard to acromegaly, however, whereas there is obvious growth of acral parts and vertebrae, there also is a marked *osteoporosis* in the skeleton, particularly in the long bones and the pelvis; hence, the author lists acromegaly in Table 3 as one of the causes of *osteoporosis.* In his second subheading, *Increased Osteoblastic Activity,* as well as in his third subheading, *Decreased Osteolytic Activity,* Follis brings out the difference in the response of bones to estrogen in the mouse as compared with the rat; this has been demonstrated by many investigators.[3,7,12]

The third subheading of Follis, *Decreased Osteolytic Activity,* corresponds to that given by the author in Table 2 as "Too Little Resorption of Matrix and Calcium," since *marble bone disease* is another term for *osteopetrosis.* Follis fails to include here or elsewhere in his classification *hypoparathyroidism* (see Table 7), which has been shown[4] to produce too much calcified bone because of too little resorption of bone (decreased osteolytic activity).

The fourth subheading of Follis, *Increased Osteolytic Activity,* resembles that given by the author in Table 2 as "Too Much Resorption of Matrix and Calcium." However, the author does not agree with the inclusion of Paget's disease of bone under this subheading, because this condition is a

localized disease instead of a systemic or a metabolic bone disorder, since there always is some normal uninvolved bone (see p. 32). At the same time, the author recognizes[10] that in Paget's disease of bone the initial lesion is bone destruction (increased osteolytic activity), that the osseous involvement may be very extensive and that the condition may result in important metabolic complications (see p. 33).

In general, the author believes that the classification of Follis is useful as a scheme for organizing the causes and the mechanisms; however, it does not name the pathologic bone disorders. The author believes that the classification in Table 2 which names the specific metabolic bone disorder is probably of greater value to the clinician who visualizes bone as he sees it calcified in roentgenograms.

Classification of Babaiantz. Babaiantz[2] has proposed a complicated classification with ten headings that deals with the causative factors without describing the bone disease. He includes such items as Sudek's atrophy, splanchnic osteopathy, toxic osteodystrophy and so forth.

Classification of Haldeman. Haldeman[9] has divided bone diseases into two main groups — *Osteolysis* and *Osteosclerosis*. Then he subdivides each into *generalized* and *localized* disorders. This classification may have some merit for radiologists for descriptive purposes, but it is of little assistance to the clinician from the point of view of the pathologic physiology or mechanism of the osseous disorder.

Classification of Stein, Stein and Beller. Stein, Stein and Beller[11] have classified Generalized Diseases of Bone under three headings. Bone-Formative Lesions; Bone-Absorptive Lesions; and Mixed Lesions No further organization of metabolic osseous disorders is attempted. These investigators have provided a similar classification for Localized Bone Lesions and for Disseminated Bone Lesions. As they indicate, their system of classification is descriptive and primarily of value to the radiologist; it is of limited usefulness to the clinician interested in the pathologic physiology of the osseous disturbances.

SUMMARY

Metabolic bone disorders are osseous disturbances resulting from generalized or systemic diseases; they are to be distinguished from localized bone disorders. Problems arise in differentiating these two conditions because it is difficult to detect the early stages or the mild states of generalized involvement and to recognize the true nature of generalized disturbances with prominent localized manifestations, of localized disorders with extensive or widely disseminated lesions and of localized osseous conditions with generalized metabolic derangements superimposed upon them.

The concepts and the terms employed to indicate the specific metabolic bone disorders should be defined carefully in each presentation concerning these conditions in an effort to reduce the confusion that now exists in terminology. The nomenclature should be chosen so that it is applicable throughout the course of the specific metabolic bone disease entity under discussion. Pathologic terms should not be used to describe physiologic processes. Certain words, such as *decalcified* and *demineralized* should be avoided; they have been misused so consistently that they have lost much of their meaning. The author gives his concepts and nomenclature in detail and proposes the new terms *normomass, hypomass* and *hypermass* to describe the status of "the total amount of the calcified bone mass," and also the terms *normopaque, hypopaque* and *hyperpaque* to describe the status of "the density of the bone image in roentgenograms."

The finding of bone hypopacity and deformity in roentgenograms is of considerable value in indicating the presence of a metabolic bone disturbance, but is of little value in establishing the nature of the specific disease entity, since the same structural abnor-

malities can occur in any of the several osseous disorders with too little calcified bone. Greater assistance in establishing the specific diagnosis from the films is obtained from the finding of associated manifestations (such as cysts, bending, spontaneous fractures or pseudofractures) or of involvement in particular areas of the skeleton that are found characteristically in a specific disorder.

A classification of metabolic bone disorders is presented in terms of the alterations in the total mass of calcified bone and the status of the bone-forming and the bone-resorbing processes. The following specific metabolic bone disorders are included: *osteoporosis; osteomalacia; osteitis fibrosa generalisata; hyperosteogenesis;* and *osteosclerosis.* The definitions and the causes of these disorders are considered. The proposals of certain other workers for classifying metabolic bone disorders are discussed briefly.

REFERENCES

1. Albright, F., and Reifenstein, E. C., Jr.: *The Parathyroid Glands and Metabolic* Bone Disease: Selected Studies, Baltimore, Williams & Wilkins, 1948.
2. Babaiantz, L.: The osteoporoses, Schweiz. med. Wchnschr. 78:340, 1948.
3. Day, H. G., and Follis, R. H., Jr.: Skeletal changes in rats receiving estradiol benzoate as indicated by histological studies and determinations of bone ash, serum calcium, and phosphatase, Endocrinology 28:83-93, 1941.
4. Emerson, K., Jr., Walsh, F. B., and Howard, J. E.: *Idiopathic hypoparathyroidism;* a report of two cases, Ann. Int. Med. 14: 1256-1270, 1941.
5. Follis, R. H., Jr.: Nutrition and bone disease, J. Mt. Sinai Hosp. 16:1-13, 1949.
6. ———: *The influence of essential nutrients* and hormones on cartilage and bone *in* Tr. of Conf. on Metabolic Interrelations with Special Reference to Calcium, vol. 2, pp. 221-257, New York, Macy, 1950.
7. Gardner, W. U., and Pfeiffer, C. A.: *Influence* of estrogens and androgens on the skeletal system, Physiol. Rev. 23:136-165, 1943.
8. Haldeman, K. O.: Factors determining the *deposition and demineralization of bone,* J. Bone & Joint Surg. 32A:596-600, July 1950.
9. Reifenstein, E. C., Jr.: Section 3—Metabolic Disorders of Bone, Ch. 97—General *considerations in Harrison,* T. R. (ed.): Principles of Internal Medicine, ed. 2, pp. 697-698, New York, Blakiston Division of McGraw-Hill, 1954.
10. Reifenstein, E. C., Jr., and Albright, F.: *Paget's disease: its pathologic physiology and the importance of this in the complications arising from fracture and immobilization,* New England J. Med. 231:343-355 and 525 (correction), 1944.
11. Stein, I., Stein, R. O., and Beller, M. L.: Living Bone in Health and Disease, Philadelphia, Lippincott, 1955.
12. Urist, M. R., Budy, A. M., and McLean, F. C.: *Species differences in the reaction of* the mammalian skeleton to estrogens, Proc. Soc. Exper. Biol. & Med. 68:324-326, 1948.

Le Definitiones, le Terminologia, e le Classification de Metabolic Disordines Ossee

Summario in Interlingua

Metabolic disordines ossee es disturbationes in le ossos que resulta de morbos generalisate o systemic. *Illos debe esser* differentiate ab localisate disordines ossee. Le differentiation inter iste duo conditiones presenta multe problemas proque il es difficile deteger le prime phases del statos de leve affectiones generalisate e recognoscer le ver natura de disturbationes generalisate que ha prominente manifestationes localisate, de disordines localisate que se manifesta in extense o multo disseminate lesiones, e de

localisate conditiones ossee super le quales generalisate disordines metabolic es superimponite.

Le conceptos e le terminos usate in le designation de specific metabolic disordines ossee debe esser cautemente definite in omne presentation individual pro reducer le confusion que nunc existe in le terminologia de iste conditiones. Le nomenclatura debe esser seligite de maniera que illo remane applicabile durante le integre curso del specific metabolic morbo ossee sub discussion. Terminos pathologic non debe esser usate in le description de processos physiologic. Certe terminos, per exemplo *discalcification* e *dismineralisation*, debe esserevitate, proque illos ha essite abusate si regularmente que illos ha perdite un grande parte de lor signification. Le autor presenta su conceptos e su nomenclatura in detalio. Ille propone le nove terminos *normamassa*, *hypomassa* e *hypermassa* pro describer le stato del "total quantitate de calcificate massa ossee" e etiam terminos *normo-opac*, *hypo-opac* e *hyper-opac* pro describer le stato del "densitate del configuration ossee in le roentgenogramma."

Le constatation de hypo-opacitate e de deformitate ossee in roentgenogrammas es de valor considerable in le indication del presentia de metabolic disturbationes ossee, sed illo es de pauc valor in le establimento del natura del specific entitate pathologic, proque le mesme anormalitates structural pote occurrer in plure differente disordines ossee que es equalmente characterisate per un insufficientia de osso calcificate. Adjuta in establir le diagnose super le base del roentgenogrammas pote esser obtenite in le constatation de associate manifestationes (per exemplo de cystes, de curvature, de fracturas spontanee, o de pseudofracturas) o in le constatation del affection de areas specific del skeleto si tales es characteristic de disordines particular.

Es presentate un classification de metabolic disordines ossee super le base del alterationes del massa total de osso calcificate e del stato del processos de formation e resorption del osso. Le sequente specific metabolic disordines ossee es includite: osteoporosis, osteomalacia, osteitis fibrose generalisate, hyperosteogenesis e osteosclerosis. Le definitiones e le causas de iste disordines es discutite. Es presentate un breve discussion del proponimentos de certe altere autores relative al classification de metabolic disordines ossee.

5

The Parathyroid Hormone and Bone*

FRANKLIN C. MCLEAN, M.D.†

Modern knowledge of the relationships of the parathyroid hormone to the physiology of bone dates from the isolation of an active extract of the glands, accomplished independently by Hanson[27,28] and by Collip[15], and from the first parathyroidectomy performed by Mandl in 1922.[45] Since that time there have been numerous reviews, which may be consulted for a general and extensive treatment of the subject.[1,3,6,8,11,16,20,21,23,24,25,39,43,44,47,48,51,57]

Mandl's parathyroidectomy and the isolation of an active parathyroid extract opened the way for both experimental and clinical studies of the function of the parathyroid glands, and there have been many advances. In spite of the improved understanding of the physiology, the pathology and the pathologic physiology of these glands, there still are areas of uncertainty; moreover, the parathyroid hormone has not been isolated in pure form, and the available extracts of the glands have not proved to be reliable tools in the management of hyperparathyroidism.

PATHOLOGY OF THE PARATHYROID GLANDS

The pathologic changes in the parathyroid glands in hyperparathyroidism have been divided sharply into two types, neoplasia and hyperplasia.[13] Localized tumors of a single gland, part of a gland or, rarely, parts of two glands are to be regarded as neoplasms. There is a roughly quantitative relation between the size of the enlarged glands and the degree of hyperfunction. Glands weighing as much as 250 Gm. have been reported; others described but not weighed may have been even larger. Neoplasms of the parathyroids are commonly adenoma.[7,13,61] Primary carcinoma, resulting in hyperparathyroidism, and in metastases, is rare.[62]

Secondary hyperparathyroidism, with hyperplasia of the parathyroid glands, occurs when there is an abnormal stimulus to parathyroid activity, resulting from a tendency to hypocalcemia. This condition is seen clinically in dietary deprivation of calcium, in pregnancy and lactation, in rickets and osteomalacia, and in chronic nephritis. It has been produced experimentally in animals by a diet either low in calcium or high in phosphate.[12]

The characteristics of primary parathyroid hyperplasia, sometimes called hypertrophy,[3] have been described.[13] There is diffuse, uniform enlargement of all the glandular tissue, a total of 15.6 Gm. of parathyroid tissue having been removed from one patient; this is one hundred times the weight of the normal parathyroid tissue of adult man and represents a degree of hyperplasia not equalled by the enlargement of any other gland of the body. Such enlargement, however, is rare in secondary hyperplasia.

THE PARATHYROID HORMONE

The parathyroid hormone has not been prepared in pure form. Parathyroid Extract, U.S.P., contains the water-soluble fractions

* Aided by a grant from the Josiah Macy, Jr. Foundation

† Department of Physiology, The University of Chicago

of the glands. It is standardized biologically so that 1 cc. contains 100 (Hanson) units; each unit is 1/100 of the amount required to raise the calcium level of the blood serum of normal, healthy male dogs weighing 10 to 12 Kg. by an amount of 1 mg. per 100 cc. Five U.S.P. or Hanson units are equivalent to 1 Collip unit; the Collip unit is still in use in some parts of the world.

MODE OF ACTION OF THE PARATHYROID HORMONE

Two views of the mode of action of the parathyroid hormone on bone were introduced within a few years after isolation of an active extract of the glands; until recent years the subject has remained controversial. The first hypothesis was advanced by Albright and Ellsworth in 1929,[2] based on observations of the response of a single patient with idiopathic hypoparathyroidism to administration of parathyroid extract. It was found that administration of the extract led first to increased excretion of phosphate in the urine; it was concluded that the increase in serum calcium, the increase in calcium excretion and the decrease in serum phosphorus, all of which also followed administration of the extract, were the sequelae of the increase in phosphate excretion. The hypothesis was that the lowering of the serum-phosphate level led to unsaturation of the blood with calcium phosphate and that this was met by mobilization of calcium from the bones.

The second view—that the parathyroid hormone acts directly on bone, inducing resorption and consequent liberation of calcium into the circulation—was advanced in 1932 by Thomson and Pugsley,[58] who concluded that the parathyroid hormone directly *stimulated* the osteoclastic process in bone. They based this conclusion on their failure to support the hypothesis of Albright and Ellsworth[2] and on the histologic evidence brought forward by others.[9,34,50]

The evidence for and against the two hypotheses has been reviewed many times; no purpose will be served by repeating the arguments here. In spite of a few dissenting voices, the weight of evidence indicates that the most characteristic effects of the parathyroid hormone—hypercalcemia, resorption of bone and fibrous dysplasia of the bone marrow—can be produced in experimental animals in the absence of the kidneys. If this is correct, it rules out the necessity of an indirect effect upon bone, mediated by the kidneys; it does not invalidate the conclusion, now generally accepted, that there is a second effect of the hormone upon excretion of phosphate by the kidneys.

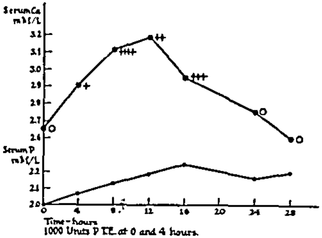


FIG. 1. Serum calcium and serum phosphate of dog and ability to produce calcification of rachitic cartilage in vitro following administration of parathyroid extract. The animal was given 1,000 units of parathyroid extract at 0 hr., and again at 4 hr. Serum withdrawn at 0, 24 and 48 hr. produced no calcification of rachitic cartilage in vitro; serum withdrawn at 4, 8, 12 and 16 hr. produced +, ++++, ++ and +++ calcification, respectively. (McLean, Lipton, Bloom and Barron: Tr. Conf. Metabolic Aspects of Convalescence 14:34)

McLean, Lipton, Bloom and Barron,[42] making use of a concept that they referred to as "biologic solubility," performed an experiment that they regarded as crucial to determine whether or not *administration* of parathyroid extract increased the solubility of the bone salt in the circulating fluids of the body, leading to its solution from bone. They administered large doses of parathyroid extract to adult dogs, the serum of which before treatment did not produce in vitro

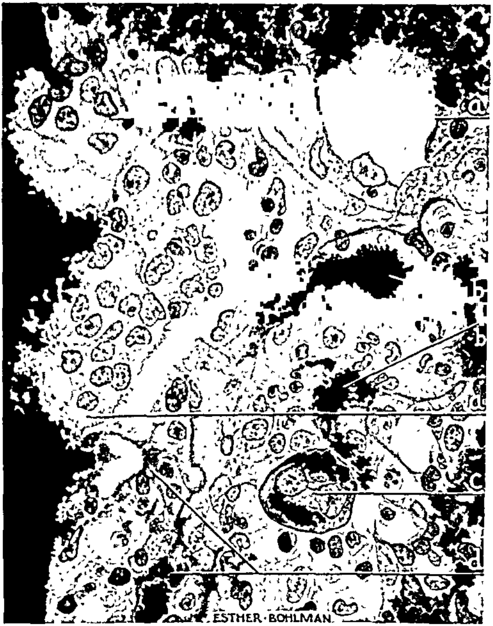


FIG. 2. High-power view from undecalcified section of a rib of a puppy 12 hr. after injection of 200 U.S.P. units of parathyroid extract per Kg. of body weight: (a) osteoclasts, free from aggregated bone salt; (b) macrophages, packed with bone salt; (c) megakaryocyte, containing bone salt; (d) basophil network. Formaldehyde fixation; silver nitrate, hematoxylin and eosin; camera lucida; × 681. (McLean & Bloom: Arch. Path. 32:6)

evidence of phagocytosis of these substances by other cells in the bone marrow in the immediate vicinity of bone undergoing resorption (Fig. 2). For the present the possibility that resorption of bone occurs by osteoclastic resorption may be excluded.

It may still be asked whether or not there is sufficient evidence to implicate the osteoclast in resorption at all. There is the possibility that this multinucleated giant cell is simply a by-product of resorption, being formed by aggregation of osteocytes and osteoblasts liberated by resorption effected by other means. An exhaustive review[26] concludes that there is no direct evidence that osteoclasts erode bone but that their constant occurrence in zones where resorption is taking place is more than incidental. The influences that evoke and control osteoclastic activity may be found either generally, throughout the organism, or locally, in circumscribed areas. Here we are concerned with the humoral control of resorption, especially as it is mediated through the parathyroid glands.

ROLE OF THE PARATHYROID GLANDS IN HOMEOSTASIS

It is firmly established that the parathyroid glands play a decisive role in the homeostatic regulation of the calcium-ion concentration of the blood plasma. There is a direct cor-

mates that in an ultrafiltrate of plasma. In such fluids the concentration of calcium is normally about 5 mg. per 100 cc. (1.25 mM. per liter), virtually all diffusible. Again, a fraction of this may be in the form of un-ionized diffusible complexes; these have little or no physiologic significance.

THE PHOSPHATES OF THE FLUIDS OF THE BODY

Inorganic phosphate is present in the fluids of the body in the form of the ions of orthophosphoric acid, H_3PO_4, of which more than 80 per cent is $HPO_4^{=}$.[41] The plasma of the infant, under conditions of active deposition of bone salt, contains approximately 6 mg. per 100 cc. of phosphorus as inorganic phosphate (2 mM. per liter). In the adult the inorganic phosphate level of the plasma is reduced to approximately one half of that of the infant. It is characteristic of the rachitic infant that the concentration of inorganic phosphate in the plasma is at a level normal for the adult.

Excretion of phosphate through the kidneys varies within wide limits; the amount excreted depends mainly on the intake. Homeostatic control of the plasma-phosphate level, mediated by the effect of the parathyroid hormone on renal excretion of phosphate, is a possibility. That the parathyroid glands respond to fluctuations in the concentration of phosphate ions in the plasma—a necessary step in such control—has been claimed.[22,30,59]

HOMEOSTATIC REGULATION OF THE CALCIUM-ION CONCENTRATION IN THE BLOOD

At all levels of calcium-ion concentration in the fluids of the body there is exchange of calcium and phosphate between the blood and the bones; in the absence of the parathyroid glands a relatively constant, although low, concentration of calcium ions is maintained in the blood. While it is clear that the parathyroid glands are necessary for the maintenance of *normal* calcium-ion levels in the blood, the relationship between their function and the occurrence of transfer of calcium between blood and bones in their absence has not been well understood. Most of the experiments bearing on this problem have been concerned with the mobilization of calcium from the bones after the blood has been partially depleted of this element; there are also observations of the effect of the parathyroid hormone upon the uptake of calcium from the blood by the bones.

Hastings and Huggins[29] withdrew blood repeatedly from dogs, replacing it with serum decalcified by shaking with lead phosphate. When the procedure was interrupted the serum calcium rose rapidly, approaching a normal level in animals with intact parathyroid glands but not exceeding a hypocalcemic level in animals previously parathyroidectomized. Patt and Luckhardt[46] confirmed and extended these observations. In addition, they administered sodium oxalate intravenously. This caused a sharp fall in the serum-calcium level, with a rapid return to normal in intact animals. When dogs were subjected to parathyroidectomy just prior to administration of sodium oxalate, the end-result was the hypocalcemic level characteristic of hypoparathyroidism. A third procedure, that of administration of ethylenediaminetetra-acetic acid (EDTA) intravenously has recently been given intensive study by Copp.[10]

Stewart and Bowen[54] developed the *oxalate tolerance curve* as a measure of parathyroid function. Their results differed from those of Hastings and Huggins and of Patt and Luckhardt, in that they observed no appreciable return of the serum calcium toward preinjection levels in parathyroidectomized animals. This led them to regard the oxalate tolerance solely as an index of the functional activity of the parathyroids. They attributed the contrary results of the previous workers to residual hormone activity, owing to the brief interval allowed to elapse following parathyroidectomy.

The experiments of Copp appear to leave no doubt that turnover of calcium in blood

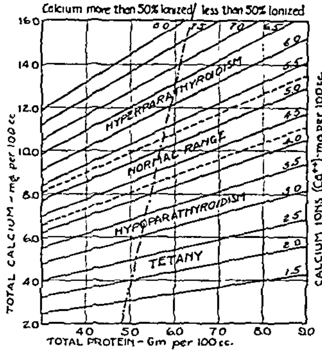


FIG. 3. Chart for calculation of Ca^{++} concentration from total protein and total calcium of serum or plasma. (McLean & Hastings: Am. J. Med. Sc. 189:601)

relation between the calcium-ion levels in the body fluids and the state of activity of the parathyroid glands. The relationship between the parathyroids and the control of phosphate concentration in the blood is less clear.

THE CALCIUM OF THE FLUIDS OF THE BODY

All or nearly all of the calcium in the blood is in solution in the plasma; the amount in the red blood cells is negligible. In normal man the concentration of calcium in the plasma is usually between 9 and 11 mg. per cc., with 10 mg. per 100 cc. (2.5 mM. per liter) a representative figure. This is in constant exchange with the calcium of the extracellular fluid and of the bones; the homeostatic mechanism that maintains the constancy of the concentration in the plasma is the function of the parathyroid glands. In the absence of the parathyroids the plasma calcium may fall to 7 mg. per 100 cc. or, even lower. In pathologic or artificially induced hyperparathyroidism the figure may reach 15 mg. per 100 cc. or higher.

It has been known since early in the present century that the calcium in the plasma is separable into two major and roughly equal fractions—diffusible and nondiffusible. It has also been known that the nondiffusible fraction is associated with the plasma protein. However, there was for some years a considerable difference of opinion concerning the diffusible fraction. It was held by many that a major portion of this fraction was in the form of a complex with the citrate ion or with some other comparable substance. These uncertainties have been resolved, and the relationship of calcium to the plasma protein has been incorporated in a formulation that describes the plasma as a solution of a partially ionized weak electrolyte, calcium proteinate, the ionized and the un-ionized fractions being in equilibrium with each other.[41]

The calculation of the concentration of the physiologically active calcium ions is facilitated by the use of a nomogram, shown in Figure 3, illustrating the relationships of the ionized and the un-ionized fractions of calcium at varying protein and calcium levels.[40] At normal protein levels, about one half of the plasma calcium is in the ionized form; the other half is in the undissociated complex with protein. This takes into account only calcium ions and the un-ionized calcium-proteinate fraction, and ignores a small amount of calcium in other combinations. Calcium forms partly ionized complexes with the ions of other acids, including citrate, phosphate and bicarbonate, but in man and in most other animals the aggregate of all un-ionized complexes in the blood, with the exception of proteinate, can hardly account for more than 5 to 10 per cent of the total calcium. When serum is subjected to diffusion, or to ultrafiltration, these complexes appear in the diffusible fraction; for this reason the total diffusible calcium is slightly higher than the calcium-ion concentration.

In the protein-poor fluids of the body, such as the cerebrospinal fluid and the intercellular fluids, the state of calcium approxi-

mates that in an ultrafiltrate of plasma. In such fluids the concentration of calcium is normally about 5 mg. per 100 cc. (1.25 mM. per liter), virtually all diffusible. Again, a fraction of this may be in the form of un-ionized diffusible complexes; these have little or no physiologic significance.

THE PHOSPHATES OF THE FLUIDS OF THE BODY

Inorganic phosphate is present in the fluids of the body in the form of the ions of orthophosphoric acid, H_3PO_4, of which more than 80 per cent is $HPO_4^{=}$.[41] The plasma of the infant, under conditions of active deposition of bone salt, contains approximately 6 mg. per 100 cc. of phosphorus as inorganic phosphate (2 mM. per liter). In the adult the inorganic phosphate level of the plasma is reduced to approximately one half of that of the infant. It is characteristic of the rachitic infant that the concentration of inorganic phosphate in the plasma is at a level normal for the adult.

Excretion of phosphate through the kidneys varies within wide limits; the amount excreted depends mainly on the intake. Homeostatic control of the plasma-phosphate level, mediated by the effect of the parathyroid hormone on renal excretion of phosphate, is a possibility. That the parathyroid glands respond to fluctuations in the concentration of phosphate ions in the plasma—a necessary step in such control—has been claimed [22,30,59]

HOMEOSTATIC REGULATION OF THE CALCIUM-ION CONCENTRATION IN THE BLOOD

At all levels of calcium-ion concentration in the fluids of the body there is exchange of calcium and phosphate between the blood and the bones; in the absence of the parathyroid glands a relatively constant, although low, concentration of calcium ions is maintained in the blood. While it is clear that the parathyroid glands are necessary for the maintenance of *normal* calcium-ion levels in the blood, the relationship between their function and the occurrence of transfer of calcium between blood and bones in their absence has not been well understood. Most of the experiments bearing on this problem have been concerned with the mobilization of calcium from the bones after the blood has been partially depleted of this element; there are also observations of the effect of the parathyroid hormone upon the uptake of calcium from the blood by the bones.

Hastings and Huggins[29] withdrew blood repeatedly from dogs, replacing it with serum decalcified by shaking with lead phosphate. When the procedure was interrupted the serum calcium rose rapidly, approaching a normal level in animals with intact parathyroid glands but not exceeding a hypocalcemic level in animals previously parathyroidectomized. Patt and Luckhardt[46] confirmed and extended these observations. In addition, they administered sodium oxalate intravenously. This caused a sharp fall in the serum-calcium level, with a rapid return to normal in intact animals. When dogs were subjected to parathyroidectomy just prior to administration of sodium oxalate, the end-result was the hypocalcemic level characteristic of hypoparathyroidism. A third procedure, that of administration of ethylenediaminetetra-acetic acid (EDTA) intravenously has recently been given intensive study by Copp.[19]

Stewart and Bowen[54] developed the *oxalate tolerance curve* as a measure of parathyroid function. Their results differed from those of Hastings and Huggins and of Patt and Luckhardt, in that they observed no appreciable return of the serum calcium toward preinjection levels in parathyroidectomized animals. This led them to regard the oxalate tolerance solely as an index of the functional activity of the parathyroids. They attributed the contrary results of the previous workers to residual hormone activity, owing to the brief interval allowed to elapse following parathyroidectomy.

The experiments of Copp appear to leave no doubt that turnover of calcium in blood

and bone may occur independently of parathyroid activity. Copp injected EDTA intravenously in dogs at a constant rate over a period of time, with frequent observations of the concentration of nonchelated serum calcium, which fell rapidly during the injections. Then he permitted recovery to occur and found that the preinjection level of serum calcium was reached rapidly. From his data he calculated the rates of mobilization of calcium from the bones. From these data also, by making the assumption that the blood passing through the bone in contact with the bone mineral was restored to the preinjection level of calcium during one passage, he was able to calculate the rate of blood flow through the bones; this is an application of the principle of clearance in reverse.

Copp then repeated the same observations in parathyroidectomized dogs. Making the same assumptions, his calculations indicated that the rate of blood flow through bone tissue was not changed by removal of the parathyroids. Calculation of the rate of mobilization of calcium from bone to blood also indicated no change in the parathyroidectomized animals.

Talmage, Kraintz and Kraintz[56] studied the effect of the parathyroids on calcium uptake and exchange in the rat, observing the rates of disappearance of Ca-45 from the plasma and of its uptake in the bones following intraperitoneal administration in normal and in parathyroidectomized rats. They found that the uptake of calcium by bone was not altered significantly in the parathyroidectomized animals during the first 6 hours—which they called the exchange period—but that the turnover of calcium in the bones was at a significantly lowered rate in the absence of the parathyroids after 6 hours, in what they called the "turnover rate" portion of the curve (Fig. 4). However, their curves for both the earlier and the later periods during which observations were made are more remarkable for the similarity of the response of normal and of parathyroidectomized animals than for any dissimilarities, indicating that the turnover of calcium in blood and bone continues at a high rate after removal of the parathyroids. The

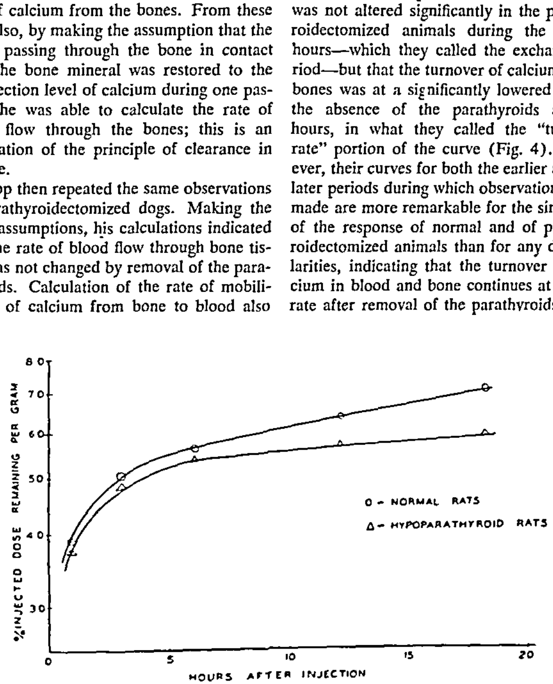


FIG. 4. Uptake of Ca-45 in bone of normal and hypoparathyroid rats after administration of 20 μc carrier-free Ca-45. (Talmage, Kraintz & Kraintz: Proc. Soc Exper. Biol. & Med 80:553)

lower rate of uptake by the bones of parathyroidectomized rats after 6 hours may well have been the result of equilibrium with the lower concentration of calcium in the serum of these animals during this period.

In a more recent paper Talmage and Elliott[37] have reported on changes in extracellular fluid levels of calcium in nephrectomized rats following parathyroidectomy; their observations were made on fluid introduced into the peritoneal cavity and permitted to come into equilibrium with the blood. They found that in rats with intact parathyroids the calcium concentration of the fluid was maintained at a level between 6 and 6.8 mg. per 100 cc., while after parathyroidectomy this was reduced to between 3.5 and 4 mg. per 100 cc.; in both cases the concentration remained constant between the limits reported.

Comar[17] also has found that in parathyroidectomized rats calcium may be removed from the body by intraperitoneal lavage, with the blood level being maintained at that characteristic of parathyroidectomy.

All these observations lead to the conclusion that there is rapid movement of calcium ions, in both directions, between the bones and blood. The parathyroids are essential for maintenance of a normal level of calcium in the blood, and this is accomplished by the influence of the parathyroid hormone on the mobilization of calcium from the bones; the weight of evidence is to the effect that the parathyroid hormone does not play any role in the uptake of calcium by the bones. A distinction must be drawn between (1) a mechanism acting in one direction only, i.e., mobilization of calcium from the bones under the influence of the parathyroid glands, and (2) the transfer of calcium between blood and bone, in both directions, independently of parathyroid function. These two closely related phenomena have been

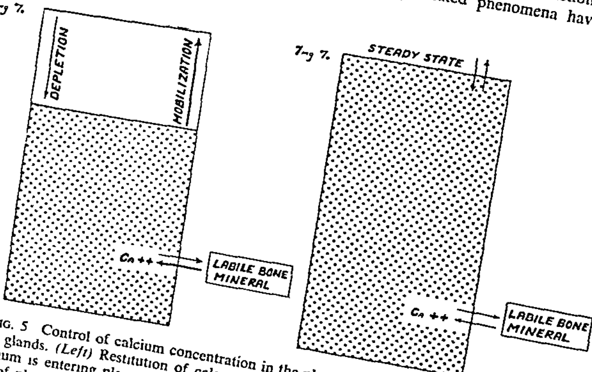


FIG. 5 Control of calcium concentration in the plasma in the absence of the parathyroid glands. *(Left)* Restitution of calcium concentration in plasma following depletion. Calcium is entering plasma from labile fraction of mineral in the bones, resulting in a rise of plasma calcium level. *(Right)* Steady state has been reached as a result of movement of calcium from bone to blood as shown at left. Calcium concentration in plasma is maintained at a level of approximately 7 mg. per 100 cc. by equilibrium with labile mineral of the bone. Under these conditions turnover of calcium in blood and bone continues at a rapid rate, without change in net distribution.

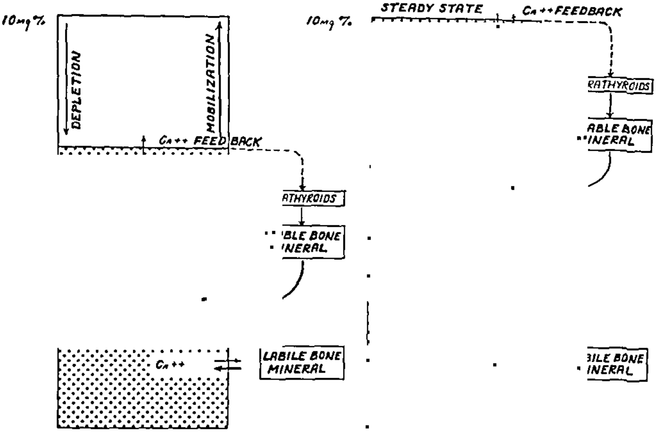


Fig. 6. Control of calcium concentration in the plasma in the presence of normally functioning parathyroid glands *(Left)* Restitution of calcium concentration in plasma following depletion, by mobilization of calcium from the bones. Calcium is entering plasma from labile fraction of mineral in the bones by diffusion, and additional calcium is added to plasma by mobilization of stable fraction, resulting from effect of parathyroid hormone, under control of feedback mechanism, activated by lowered concentration of Ca^{++} in the plasma. *(Right)* Steady state has been reached as a result of movement of calcium from bone to blood as shown at left. Calcium concentration in plasma is maintained at a level of approximately 10 mg. per 100 cc.

brought into a single framework by means of the concept of a dual mechanism, both parts of which are essential to the regulation or control of the calcium-ion level in the blood plasma.[43]

Of the dual mechanism, one part acts by diffusion equilibrium between the plasma and the labile fraction of the bone mineral. This part of the mechanism, in the absence of the parathyroid glands, is adequate to effect rapid exchange between the blood and the bones and to maintain the plasma-calcium level at approximately 7 mg. per 100 cc. (Fig 5) The second part of the dual mechanism is dependent upon mediation by the parathyroid glands and is best understood in terms of "feedback." This means simply a self-regulating process, by which information about the output is fed back to an earlier stage, so as to influence its action and hence to change the output itself. In the case of regulation of the calcium-ion concentration in the plasma, a falling level of calcium ions provides a stimulus to the parathyroid glands, resulting in an increased output of the parathyroid hormone. This in turn brings about an increase in the mobilization of calcium from the bones and a consequent increase in the calcium level of the plasma (Fig. 6).

The parathyroid hormone causes destruction of both the mineral and organic components of bone, and the feedback mechanism releases calcium from the stable as well as from the labile fractions of the bone mineral. According to this interpretation, the labile

fraction of the calcium of the mineral is easily accessible to ionic exchange with the fluids of the body. On the other hand, the stable fraction of calcium does not dissolve readily and requires the action of the parathyroid hormone for its liberation.

If one regards the plasma calcium as in equilibrium with the labile fraction of the bone mineral, as is now commonly assumed, it will be noted that the parathyroid hormone, under physiologic conditions, has the effect of raising the equilibrium point from the approximately 7 mg. per 100 cc. characteristic of the absence of the parathyroids to the normal of 10 mg. per 100 cc. This is to say that the parathyroid hormone releases enough stable calcium to raise the plasma level from 7 to 10 mg. per 100 cc. and to hold it at this level, and that the difference is, in effect, added to the labile fraction. The minute-to-minute adjustments in plasma-calcium level then are made by diffusion between blood and bone, and changes in parathyroid activity need to come into play only for adjustment over longer periods of time.

The summation of the effects of the two components of the dual mechanism is comparable with the maintenance of a constant temperature in a water bath. For example, if it is desired to operate a water bath at 38° C. in a room with a temperature of 20° C., it is common practice to supply the greater amount of the heat required from a constant source, adequate to keep the temperature of the bath at, say, 33° C. Above this temperature the additional heat required is under the control of a thermoregulator, itself under the influence of the temperature of the water. The constant source of heat is comparable with the supply of calcium to the blood by diffusion from the labile fraction of the bone mineral, the heat under control of the thermoregulator is comparable with the supply of calcium regulated by the parathyroid glands In both cases accurate regulation is brought about through a feedback mechanism, the effects of which are added to those of a second mechanism that requires no regulation. From this point of view the parathyroids may be regarded as an analog of a thermoregulator. The setting of the regulator, the parathyroid glands, is fixed, under physiologic conditions; it is raised in hyperparathyroidism and lowered in hypoparathyroidism.

THE PARATHYROIDS AND BONE DISEASE

Reports on the effects of hypofunction of the parathyroid glands on bones are conflicting; it has been reported that the density of the skeleton is somewhat increased in this condition.[3,73] Changes in the skeleton may be regarded as negligible in the total picture of hypoparathyroidism.

The sequence of events in the bones, under the influence of an excess of parathyroid hormone, is studied best in experimental animals, and more particularly in young growing animals. The advanced changes of chronic hyperparathyroidism may be seen only in man, since the rapid development of resistance to parathyroid extract prevents experimental production and maintenance of the chronic condition.

The gross skeletal changes in chronic hyperparathyroidism in man are those of softening of the bones, with consequent deformities and fractures.[18,32,33,52] The diagnosis may be suggested by the deformities and by the roentgenographic evidence of generalized decrease in the density of the bones, often accompanied by cysts and tumors. The microscopic findings are those of greatly increased resorption of bone, with numerous osteoclasts. These are accompanied by increased osteoblastic activity, indicative of attempts to repair the damaged trabeculae of bone. Attempts at repair also result in an excess of fibrous connective tissue; this has led to the use of the term *osteitis fibrosa* to describe the pathologic changes in the bones. Such bone matrix as is present, old and new, is calcified; it is not correct to refer to the changes in the bones as decalcification. There may be large fibrous scars in areas formerly occupied by spongy bone. Some of

these scars are brown, owing to their content of blood pigment, and they may contain multinucleated giant cells; from these characteristics they have been called brown tumors, giant-cell tumors or osteoclastomas.

If biopsies of bone are performed after the removal of hyperfunctioning parathyroid tissue, it is seen that reparative changes take place rapidly. Fibrous tissue is removed, and is replaced by new bone which assumes a normal appearance. Actual cysts in bone may remain unless dealt with surgically.

Cases of severe hyperparathyroidism without bone disease have been described.[4] The distinction is clinical rather than pathologic, since few such patients come to autopsy. A distinguishing feature is that, unless bone disease is present, the serum alkaline phosphatase level is within normal limits, whereas when bone changes are in progress the phosphatase level is elevated. Bone changes may be prevented or alleviated by increasing the intake of calcium, and therapy with calcium may lead also to lowering of the serum phosphatase to normal levels; a high intake of calcium may protect the skeleton against serious damage from hyperfunction of the parathyroid glands.

Hyperparathyroidism, with or without demonstrable bone disease, frequently is accompanied by pathologic conditions other than those found in the parathyroid glands and in the bones. *Metastatic calcification* occurs in soft tissues and is especially harmful in the kidneys or in the walls of blood vessels; such calcium deposits are commonly associated with severe disease of the bones, and they reflect a condition of mobilization of the bone salt and supersaturation of the blood with this mineral, similar to that described[39] in experimental animals. Renal calculi are a frequent complication of hyperparathyroidism; they are not dependent upon changes in the bones and reflect instead the increase in renal excretion of calcium resulting from hypercalcemia. In many instances the occurrence of renal calculi is the first finding to call the attention of the clinician to the possibility of hyperparathyroidism.

Usually, the severe changes in the bones observed in experimental animals have resulted from administration of toxic doses of parathyroid extract[10,31]—doses sufficient in many instances to lead to widespread necrosis of the cellular elements of bone and bone marrow. The degree to which these findings may be extrapolated to physiologic conditions, or even to clinical hyperparathyroidism, remains in doubt. For the most part they correspond to what Albright and Reifenstein[3] have designated as parathyroid poisoning or hyperhyperparathyroidism, which they attribute to a mechanism different from that induced by smaller doses of the extract. A parallel may be found in the differences between the effects of vitamin D in prophylactic doses (1,000 I.U. per day) and in toxic or subtoxic doses (50,000 I.U. per day or more).[36] The observation of the resorption of bone in contact with transplants of parathyroid tissue[5,14] supplies a link between strictly physiologic conditions and those in the toxic range.

CLINICAL MANIFESTATIONS OF HYPERPARATHYROIDISM

The clinical findings in hyperfunction have been listed[3] under three main headings: (1) skeletal changes; (2) involvement of the kidneys; and (3) the effects of hypercalcemia. In an individual instance of hyperparathyroidism these manifestations may be present singly or in combination of two or of all three. With improvement in the recognition of the underlying condition, it is noteworthy that in a majority of cases the disease now is recognized before advanced skeletal changes are present.

The skeletal changes, demonstrable by roentgenograms, vary from minimal absorption of bone, often limited in extent, to widespread reduction in density of the skeleton, at times amounting to almost complete erasure. Associated with the more severe manifestations of the disease there usually are deformities, resulting from the lack of support from mineralized bone, often with

pathologic fractures. Cysts and osteoclastomas or a giant-cell epulis in the jaw may be found. Attention may be directed to the skeleton by pain in the bones before changes demonstrable by roentgenogram are present.

The most common form of involvement of the kidneys is the occurrence of renal stones, composed mainly of calcium and phosphate. In many instances the presence of stones in the kidney leads to further examinations resulting in the diagnosis of hyperparathyroidism. Metastatic calcification in the parenchyma of the kidneys may produce extensive destruction and may lead to difficulties in arriving at a correct diagnosis.

The finding of an increased concentration of calcium in the serum is presumptive evidence of hyperparathyroidism. Whenever the total calcium in the serum is 11 mg. per 100 cc. or higher, this calls for repetition of the analysis and for further examinations. While both the calcium-ion concentration and that of calcium associated with protein are elevated, the increase in calcium-ion concentration is characteristic of hyperparathyroidism; increase in calcium proteinate may occur also in multiple myeloma. Complete examination of the blood for evidence of hyperparathyroidism should include analysis for total protein, estimation of calcium-ion concentration from total calcium and total protein (see nomogram, Fig. 3), serum phosphate and serum alkaline phosphatase. Calcium excretion in the urine, with the patient on a low calcium intake, may exceed the usual normal limit of 150 mg. in 24 hours and may be as high as 500 to 600 mg. daily. Increase in excretion of phosphate in the urine also occurs, but may be difficult to recognize unless the patient is on a measured intake of phosphorus.

SUMMARY

This chapter summarizes current knowledge concerning the relationships of the parathyroid hormone to bone. Special emphasis is given to the following subjects:

1. It is concluded that the parathyroid hormone has a direct action upon bone tissue, leading to resorption; there is convincing evidence that a primary action upon the kidneys is not essential to the effects upon bone.

2. A hypothesis for a mechanism of the resorption of bone is proposed, providing for solution of the bone mineral, collagen and ground substance—all at the hydrogen-ion concentration of the body fluids. This hypothesis assumes that a substance having a strong affinity for calcium is responsible for solution of the bone mineral.

3. Homeostatic regulation of the calcium-ion concentration in the blood is attributed to a dual mechanism. There is a rapid movement of calcium ions in both directions between the blood and the bones independent of the parathyroid glands, and the equilibrium between the blood and the labile fraction of the bone mineral is adequate to maintain the serum-calcium level at approximately 7 mg. per 100 cc. The parathyroid hormone, acting in one direction only, by mobilization of the bone mineral, has the effect of raising the serum-calcium level to approximately 10 mg. per 100 cc. and of accomplishing regulation at this level by means of a feedback mechanism; the calcium-ion level serves as a stimulus to the parathyroids, leading to control of the output of calcium into the blood.

4. A brief résumé is given of the relation of the parathyroids to bone disease and of the clinical manifestations of hyperparathyroidism.

REFERENCES

1. Albright, F.: The parathyroids—physiology and therapeutics, J.A.M.A. 117:527, 1941.
2. Albright, F., and Ellsworth, R.: Studies on the physiology of the parathyroid glands: I. Calcium and phosphorus studies on a case of idiopathic hypoparathyroidism, J. Clin. Invest. 7:183, 1929.
3. Albright, F., and Reifenstein, E. C., Jr.: The *Parathyroid* Glands and Metabolic Bone Disease, Baltimore, Williams & Wilkins, 1948.
4. Albright, F., Sulkowitch, H. W., and Bloomberg, E.: Further experience in the diagnosis of hyperparathyroidism, including a discussion of cases with a

degree of hyperparathyroidism, Am. J. M. Sc. 193:800, 1937.
5. Barnicot, N. A.: The local action of the *parathyroid and other tissues on bone in* intracerebral grafts, J. Anat. 82:233, 1948.
6. Bartter, F. C.: The parathyroids, Ann. Rev. Physiol. 16:429, 1954.
7. Black, B. K., and Ackerman, L. V.: Tumors of the parathyroid; a review of 23 cases, Cancer 3:415, 1950.
8. Black, B. M.: Hyperparathyroidism, Springfield, Ill., Thomas, 1953.
9. Bülbring, E.: Über die Beziehungen zwischen Epithelkörperchen, Calciumstoffwechsel und Knochenwachstum, Arch. exper. Path. u. Pharmakol. 162:209, 1931.
10. Burrows, R. B.: Variations produced in bones of growing rats by parathyroid extracts, Am. J. Anat. 62:237, 1938.
11. Campbell, I. L., and Turner, C. W.: The *Relation of the Endocrine System to the* Regulation of Calcium Metabolism, Res. Bull. 352, Univ. of Missouri, Agric. Exper. Station, 1942.
12. Carnes, W. H., Pappenheimer, A. M., and Stoerk, H. C.: Volume of parathyroid glands in relation to dietary calcium and phosphorus, Proc. Soc. Exper. Biol. & Med. 51:314, 1942.
13. Castleman, B., and Mallory, T. B.: The pathology of the parathyroid gland in hyperparathyroidism; a study of 25 cases, Am. J. Path. 11:1, 1935.
14. Chang, H. Y.: Grafts of parathyroid and other tissues to bone, Anat. Rec. 111:23, 1951.
15. Collip, J. B.: The extraction of a parathyroid hormone which will prevent or control parathyroid tetany and which regulates the level of blood calcium, J. Biol. Chem. 63:395, 1925.
16. ———: The parathyroid glands, Harvey Lect. 21:113, 1925-26.
17. Comar, C. L.: Personal communication.
18. Compere, E. L.: Bone changes in hyperparathyroidism, Surg., Gynec. & Obst. 50: 783, 1930.
19. Copp, D. H.: Personal communication.
20. Dent, C. E.: Physiology of the parathyroid glands, Proc. Roy Soc. Med. 46:291, 1953.
21. Dragstedt, L. R.: The physiology of the *parathyroid glands, Physiol.* Rev. 7:499, 1927.
22. Engfeldt, B.. Studies on parathyroidal function in relation to hormonal influences and dietetic influences, Acta endocrinol. 5: 1-118 (Supp 6). 1950
23. Escamilla, R. F The parathyroid glands *in* Sloan, L. H. (ed.). Tice's Practice of Medicine, vol. 8, p. 263, Hagerstown, Md., Prior, 1954.
24. Gilmour, J. R.: The Parathyroid Glands *and Skeleton in Renal Disease*, London, Oxford, 1947.
25. Greep, R. O.: The chemistry and physiology of the parathyroid hormone *in* Pincus, G., and Thimann, K. V. (eds.): *The Hormones*, vol. 1, p. 255, New York, Acad. Press, 1948.
26. Hancox, N. M.: The osteoclast, Biol. Rev. 24:448, 1949.
27. Hanson, A. M.: An elementary chemical study of the parathyroid glands of cattle, Mil. Surgeon 52:280, 1923.
28. ———: Experiments with active preparations of parathyroid other than that of the desiccated gland, Mil. Surgeon 55:701, 1924.
29. Hastings, A. B., and Huggins, C. B.: Experimental hypocalcemia, Proc. Soc. Exper. Biol. & Med. 30:458, 1933.
30. Helfet, A. J.: A new conception of parathyroid function and its clinical applications; a *preliminary report on the results of* treatment of generalized fibrocystic and allied bone diseases and of rheumatoid arthritis by aluminium acetate, Brit. J. Surg. 27:651, 1940.
31. Heller, M., McLean, F. C., and Bloom, W.: Cellular transformations in mammalian bones induced by parathyroid extract, Am. J. Anat. 87:315, 1950.
32. Hodges, P. C.: *Skeletal changes in disturb*ances of the parathyroid glands, Radiology 26:663, 1936.
33. Jaffe, H. L.: Hyperparathyroidism (Recklinghausen's disease of bone), Arch. Path. 16:63 and 236, 1933.
34. Jaffe, H. L., and Bodansky, A.: Experimental fibrous osteodystrophy (ostitis fibrosa) in hyperparathyroid dogs, J. Exper. Med. 52:669, 1930.
35. Kolliker, A.: Die normale Resorption des Knochengewebes und ihre Bedeutung für die Entstehung der typischen Knochen*formen, pp. 86, Leipzig,* Vogel, 1873.
36. McLean, F. C.: Activated sterols in the treatment of parathyroid insufficiency *in* Glandular Physiology and Therapy, p. 461, Chicago, A. M. A., 1942.
37. ———: Biochemical and biomechanical aspects of the resorption of bone, J. Peridont. 25:176, 1954.
38. ———: The parathyroid glands and bone *in* Bourne, G. H. (ed.): The Biochemistry and Physiology of Bone, p. 705, New York, Acad Press, 1956.

39. McLean, F. C., and Bloom, W.: Calcification and ossification; mobilization of bone salt by parathyroid extract, Arch. Path. 32: 315, 1941.
40. McLean, F. C., and Hastings, A. B.: Clinical estimation and significance of calcium-ion concentrations in the blood, Am. J. M. Sc. 189:601, 1935.
41. ———: The state of calcium in the fluids of the body: I. The conditions affecting the ionization of calcium, J. Biol. Chem. 108: 285, 1935.
42. McLean, F. C., Lipton, M. A., Bloom, W., and Barron, E. S. G.: Biological factors in calcification in bone *in* Tr. 14th Conf. on Metabolic Aspects of Convalescence, vol. 14, p. 9, New York, Macy, 1946.
43. McLean, F. C., and Urist, M. R.: Bone: *An Introduction to the Physiology of Skeletal Tissue*, Chicago, Univ. Chicago Press, 1955.
44. Mandl, F.: Hyperparathyroidism; a review of historical developments and the present state of knowledge on the subject, Surgery 21:394, 1947.
45. ———: Therapeutischer Versuch bei Ostitis fibrosa generalisata mittels Extirpation eines Epithelkörperchentumors, Wien. klin. Wchnschr. 38:1343, 1925.
46. Patt, H. M., and Luckhardt, A. B.: Relationship of a low blood calcium to parathyroid secretion, Endocrinology 31:384, 1942.
47. Reifenstein, E. C., Jr.: Diseases of the parathyroid glands *in* Williams, R. H. (ed): Textbook of Endocrinology, ed. 2, p. 483, Philadelphia, Saunders, 1955.
48. Reifenstein, E. C., Jr., and Howard, R. P.: The parathyroid glands *in* Glandular Physiology and Therapy, p. 351, Philadelphia, Lippincott, 1954.
49. Rubin, M., Martell, A. E., and Bersworth, F. C.: The Biological Action of Versenes, Framingham, Mass., Versenes, Inc., 1954.
50. Selye, H.: On the stimulation of new bone-formation with parathyroid extract and irradiated ergosterol, Endocrinology 16:547, 1932.
51. Shelling, D. H.: The Parathyroids in Health and in Disease, St. Louis, Mosby, 1935.
52. Snapper, I.: Medical Clinics on Bone Diseases, ed. 2, New York, Interscience, 1949.
53. Stein, I., Stein, R. O., and Beller, M. L.: Living Bone in Health and Disease, Philadelphia, Lippincott, 1955.
54. Stewart, G. S., and Bowen, H. F.: The parathyroid control of serum calcium independent of renal mediation, Endocrinology 48:568, 1951.
55. Talmage, R. V., and Elliott, J. R.: Changes in extracellular fluid levels of calcium, phosphate and citrate ions in nephrectomized rats following parathyroidectomy, Endocrinology 59:27, 1956.
56. Talmage, R. V., Kraintz, F. W., and Kraintz, L.: Effect of parathyroids on radio-calcium uptake and exchange in rat tissues, Proc. Soc. Exper. Biol. & Med. 80: 553, 1952.
57. Thomson, D. L., and Collip, J. B.: The parathyroid glands, Physiol. Rev. 12:309, 1932.
58. Thomson, D. L., and Pugsley, L. I.: On the mechanism of parathyroid hormone action, Am. J. Physiol. 102:350, 1932.
59. Törnblom, N.: On the functional relationship between the pituitary gland and the parathyroids, Acta endocrinol. 2:1-76 (Supp. 4), 1949.
60. Weidenreich, F.: Das Knochengewebe *in* von Möllendorff, W. (ed.): Handbuch der mikroskopischen Anatomie des Menschen, vol. 2, part 2, p. 465, Berlin, Springer, 1930.
61. Woolner, L. B., Keating, F. R., Jr., and Black, B. M.: Tumors and hyperplasia of the parathyroid glands; a review of the pathological findings in 140 cases of primary hyperparathyroidism, Cancer 5:1069, 1952.
62. Wray, S.: Carcinoma of the parathyroid gland, J. Path. & Bact. 66:231, 1953.

Le Hormon Parathyroide e le Ossos

Summario in Interlingua

Iste articulo summarisa le presente cognoscentias del relation de hormon parathyroide a osso. Le sequente aspectos del problema es sublineate. (1) Es concludite que le hormon parathyroide exerce un action directe super le histos ossee, resultante in resorption. Il existe datos conclusive que supporta le these que un action primari super le renes non es un condition essential del effectos ossee. (2) Es proponite un hy-

pothese in re le mechanismo del resorption ossee. Illo explica le solution del minerales, collageno, e substantia fundamental del osso al concentration del iones hydrogenic in le fluidos del corpore. Iste hypothese suppone que un substantia con forte affinitate pro calcium es responsabile pro le solution del mineral ossee. (3) Le regulation homeostatic del concentration del iones de calcium in le sanguine es attribuite a un duple mechanismo. Il existe un rapide motion de iones de calcium in ambe directiones inter le sanguine e le ossos. Iste motion es independente del glandulas parathyroide, e le equilibrio inter le sanguine e le fraction labile del mineral ossee es adequate pro mantener le nivello seral de calcium a circa 7 mg. per 100 cm.[3] Le hormon parathyroide, que mobilisa le mineral ossee in solmente un direction, ha le effecto de elevar le nivello seral de calcium a circa 10 mg. per 100 cm.[3] e de mantener iste nivello per medio de un mechanismo de action retrorse. Le nivello del iones de calcium servi como stimulo del glandulas parathyroide, e isto resulta in un regulation del liberation de calcium a in le sanguine. (4) Es presentate un breve revista del question del relation inter le glandulas parathyroide e morbos ossee e del manifestationes clinic de hyperparathyroidismo.

6

The Varieties of Rickets and Osteomalacia Associated with Hypophosphatemia

HAROLD E. HARRISON, M.D.*

A group of disorders of skeletal calcification can be separated in which hypophosphatemia is one of the fundamental physiologic defects. If the concentration of inorganic phosphate in extracellular fluids is markedly reduced, phosphate in bone matrix cannot be concentrated to levels needed for precipitation of bone salt. In the growing subject, deposition of bone salt fails to keep pace with the growth of cartilage and the formation of new matrix, so that the pathologic changes of rickets result. In the adult the failure of calcification of matrix in the metabolically active, although no longer growing, bone results in osteomalacia.

The determination of phosphate in serum is essentially a measure of inorganic phosphate in plasma and other extracellular fluids, since the concentration of organic phosphate esters in serum is extremely low. The factors that normally regulate the concentration of phosphate in plasma must be considered if the mechanisms which produce hypophosphatemia are to be understood. These factors are intake of phosphate, degree of intestinal absorption, uptake of phosphate by bone, uptake of phosphate by tissue cells and urinary excretion of phosphate.

Hypophosphatemia can result from low intake of phosphate or impaired intestinal absorption. The former is only of theoretic interest in clinical states, since the human dietary almost always contains an excess of phosphate. Hypophosphatemia and rickets can be produced experimentally in animals even in the face of adequate vitamin D intake if the dietary phosphate is sufficiently reduced. Acute hypophosphatemia may occur in the child during periods of starvation, and especially if carbohydrate is given without phosphate. The serum-phosphorus level under these conditions may be reduced to less than 1 mg. per 100 ml., which indicates that phosphorus may be taken up by metabolizing cells even though extracellular phosphate is depleted almost to the vanishing point. Serum-phosphorus levels are also reduced during acute infections, and low phosphorus intake may be a factor here, although the hypophosphatemia of infections has not been studied completely.

One of the actions of vitamin D is to increase the efficiency of intestinal absorption of both calcium and phosphorus.[11] The hypophosphatemia of vitamin D deficiency is due in part to the lessened intestinal absorption of phosphate. Absorption of phosphorus can also be reduced by feeding a great excess of cations such as calcium or aluminum, which form insoluble phosphates in the intestinal tract. However, inadequate intestinal absorption of phosphate is not the sole explanation of the hypophosphatemia of human rickets, since intestinal absorption of phosphate, even by infants with vitamin

* Pediatric Division, Baltimore City Hospital, and Department of Pediatrics, Johns Hopkins University School of Medicine.

pothese in re le mechanismo del resorption ossee. Illo explica le solution del minerales, collageno, e substantia fundamental del osso al concentration del iones hydrogenic in le fluidos del corpore. Iste hypothese suppone que un substantia con forte affinitate pro calcium es responsabile pro le solution del mineral ossee. (3) Le regulation homeostatic del concentration del iones de calcium in le sanguine es attribuite a un duple mechanismo. Il existe un rapide motion de iones de calcium in ambe directiones inter le sanguine e le ossos. Iste motion es independente del glandulas parathyroide, e le equilibrio inter le sanguine e le fraction labile del mineral ossee es adequate pro mantener le nivello seral de calcium a circa 7 mg. per 100 $cm.^3$ Le hormon parathyroide, que mobilisa le mineral ossee in solmente un direction, ha le effecto de elevar le nivello seral de calcium a circa 10 mg. per 100 $cm.^3$ e de mantener iste nivello per medio de un mechanismo de action retrorse. Le nivello del iones de calcium servi como stimulo del glandulas parathyroide, e isto resulta in un regulation del liberation de calcium a in le sanguine. (4) Es presentate un breve revista del question del relation inter le glandulas parathyroide e morbos ossee e del manifestationes clinic de hyperparathyroidismo.

6

The Varieties of Rickets and Osteomalacia Associated with Hypophosphatemia

HAROLD E. HARRISON, M.D.*

A group of disorders of skeletal calcification can be separated in which hypophosphatemia is one of the fundamental physiologic defects. If the concentration of inorganic phosphate in extracellular fluids is markedly reduced, phosphate in bone matrix cannot be concentrated to levels needed for precipitation of bone salt. In the growing subject, deposition of bone salt fails to keep pace with the growth of cartilage and the formation of new matrix, so that the pathologic changes of rickets result. In the adult the failure of calcification of matrix in the metabolically active, although no longer growing, bone results in osteomalacia.

The determination of phosphate in serum is essentially a measure of inorganic phosphate in plasma and other extracellular fluids, since the concentration of organic phosphate esters in serum is extremely low. The factors that normally regulate the concentration of phosphate in plasma must be considered if the mechanisms which produce hypophosphatemia are to be understood. These factors are intake of phosphate, degree of intestinal absorption, uptake of phosphate by bone, uptake of phosphate by tissue cells and urinary excretion of phosphate.

Hypophosphatemia can result from low intake of phosphate or impaired intestinal absorption. The former is only of theoretic interest in clinical states, since the human dietary almost always contains an excess of phosphate. Hypophosphatemia and rickets can be produced experimentally in animals even in the face of adequate vitamin D intake if the dietary phosphate is sufficiently reduced. Acute hypophosphatemia may occur in the child during periods of starvation, and especially if carbohydrate is given without phosphate. The serum-phosphorus level under these conditions may be reduced to less than 1 mg. per 100 ml., which indicates that phosphorus may be taken up by metabolizing cells even though extracellular phosphate is depleted almost to the vanishing point. Serum-phosphorus levels are also reduced during acute infections, and low phosphorus intake may be a factor here, although the hypophosphatemia of infections has not been studied completely.

One of the actions of vitamin D is to increase the efficiency of intestinal absorption of both calcium and phosphorus.[11] The hypophosphatemia of vitamin D deficiency is due in part to the lessened intestinal absorption of phosphate. Absorption of phosphorus can also be reduced by feeding a great excess of cations such as calcium or aluminum, which form insoluble phosphates in the intestinal tract. However, inadequate intestinal absorption of phosphate is not the sole explanation of the hypophosphatemia of human rickets, since intestinal absorption of phosphate, even by infants with vitamin

* Pediatric Division, Baltimore City Hospital, and Department of Pediatrics, Johns Hopkins University School of Medicine.

TABLE 1. PHOSPHORUS METABOLISM OF BREAST-FED RACHITIC INFANT AS INFLUENCED BY VITAMIN D*

PERIOD	INTAKE *mg./day*	EXCRETION *Urine* *mg./day*	EXCRETION *Stool* *mg./day*	RETENTION *mg./day*
1	106	46	26	+ 34
4†	118	22	19	+ 77
5	113	16	25	+ 72
6	121	5	33	+ 83
9	131	2	14	+115
10	127	2	13	+112

* Taken from data of Liu, S. H., *et al.*[15]
† Vitamin D begun at start of this period.

D deficiency, ordinarily is sufficient to provide for the phosphate requirements if phosphate loss in the urine were minimal. This is shown clearly by the phosphate balances of Liu and associates[15] in infants with vitamin D deficiency (Table 1). In the breast-fed rachitic infant vitamin D reduced urine-phosphate loss, and this in conjunction with increased intestinal absorption augmented phosphate retention. Similar findings occurred in the osteomalacic mothers and were associated with rise of serum phosphorus.

The regulation of serum-phosphate levels by the kidney depends on the relationship between glomerular filtration rate and renal tubular reabsorption of phosphate, since plasma phosphate is filtrable and a considerable fraction of the filtered phosphate normally is reabsorbed by the renal tubules. Marked reduction of the glomerular filtration rate leads to increased levels of phosphorus in serum. On the other hand, reduced tubular reabsorption of phosphate with normal glomerular filtration rate results in diminished concentrations of phosphorus. Renal tubular reabsorption of phosphate is low in vitamin D deficiency rickets and osteomalacia and is increased by vitamin D administration This phenomenon has been demonstrated experimentally[13] and can be shown to occur in rachitic infants (Table 2). Whether this is a direct effect of vitamin D upon renal tubular metabolism or an indirect effect mediated through parathyroid activity remains the subject of speculation. Renal tubular reabsorption of phosphate is inhibited by parathyroid hormone, so that excess parathyroid activity is associated with reduced concentrations of phosphorus in serum and lack of parathyroid activity by high levels of serum phosphorus. Therefore, Albright and Reifenstein[2] have suggested that the apparent antagonism between vitamin D and parathyroid hormone in this respect could be the result of excess parathyroid secretory activity in vitamin D deficient states with inhibition by vitamin D administration. However, more recently it has been shown that renal amino-aciduria also occurs in vitamin D deficiency states,[11] suggesting an effect of vitamin D upon the renal tubular mechanisms for reabsorption of amino-acids as well as phosphate, which may favor the hypothesis of a more direct action of vitamin D upon renal tubule cell metabolism.

TABLE 2. CALCULATED TUBULAR REABSORPTION OF PHOSPHATE IN A RACHITIC INFANT BASED ON DETERMINATIONS OF ENDOGENOUS CREATININE CLEARANCES AND URINE-PHOSPHATE EXCRETION DURING INTRAVENOUS INFUSION OF PHOSPHATE, TUBULAR REABSORPTION CALCULATED AS MG./100 ML. OF GLOMERULAR FILTRATE.

PERIOD	CREATININE CLEARANCE *ml/min*	SERUM P *mg/100 ml.*	P EXCRETED *mg/min.*	P REABSORBED *mg./100 ml. G.F.*
Active Rickets				
1	40	2.5	0.39	1.58
2	47	2.5	0.43	1.64
3	52	3.0	0.81	1.44
4	51	4.8	1.83	1.24
5	51	6.2	2.29	1.67
6	36	7.0	2.27	0.75
Healed Rickets—Following Vitamin D Treatment				
1	39	6.1	0.64	4.50
2	46	6.1	0.88	4.18
3	49	6.7	1.19	4.32
4	37	9.1	1.81	4.12

The variations of serum-phosphate levels with age may also reflect age differences

with respect to the balance between glomerular filtration rate and renal tubular reabsorption of phosphate. In the prematurely born infant, serum-phosphorus levels of 8 or 9 mg. per 100 ml. are found frequently. In the full-term infant, concentrations of this magnitude may occur, but usually the levels range between 6 and 7 mg. per 100 ml. In later infancy and childhood, the levels diminish to between 4 and 5 mg. per 100 ml. Following adolescence, the serum-phosphorus concentrations drop to the normal adult levels of 3.0 to 4.0 mg. per 100 ml. In the subject with hypopituitarism, serum-phosphate concentrations are reduced, and in hyperpituitarism with acromegaly, the serum-phosphorus levels are higher than in the normal adult.

VITAMIN D DEFICIENCY RICKETS

This nutritional disturbance, which once was so common in infants living in cities of the latitude of the northern United States or above, now is a rare clinical entity. An intake of 400 units of vitamin D per day is sufficient to prevent rickets in over 90 per cent of infants.[10] Lack of exposure to the ultraviolet radiation of sunlight is not important if this dose of vitamin D is given. Such amounts of vitamin D can be given in the form of a few drops of vitamin D concentrate or in a multivitamin preparation. Evaporated milk, which is widely used for infant feeding, is enriched with vitamin D, so that each can, which is equivalent to a quart of reconstituted milk, contains 400 units of vitamin D. Similarly, the various prepared-milk modifications for infant feeding are enriched with vitamin D Of the relatively few cases of rickets seen in Baltimore during the last decade, a number were breast-fed infants who had not been given vitamin D supplements. In some instances failure to administer vitamin D was due to the mistaken notion that human milk was adequate nutritionally in all respects and that extra vitamin D was not required The average vitamin D content of human milk is not sufficient for the infant's requirements, although it is probable that the vitamin D content of the milk can be increased by administering vitamin D to the mother or exposing her to ultraviolet radiation.

Vitamin D deficiency rickets can also occur in infants with defects of fat absorption and associated failure of absorption of fat-soluble vitamins. One cause of such malabsorption of vitamin D is exclusion of bile from the intestines, as in congenital atresia of the bile ducts, or the obstructive jaundice sometimes seen as a complication of congenital hemolytic disease of the newborn. The author also has encountered a rare instance of an apparent familial congenital defect of fat absorption. Two siblings each developed rickets by 12 months of age despite ordinary intake of vitamin D. In addition to evidence of excessive fat in the stools, the infants showed diminished prothrombin activity resulting from impairment of vitamin K absorption. A defect of vitamin E absorption also was demonstrated. Administration of larger amounts of vitamins D and K corrected the clinical and the biochemical evidences of fat-soluble vitamin deficiency. The basis for the defective absorption of fat was not adequately explained.

Sometimes erroneous diagnoses of rickets are made on the basis of skeletal changes in the rapidly growing young infant. Craniotabes, i.e., thin, easily indented areas in the skull, may be an early sign of rickets, but can also be seen in normal infants, particularly under 3 months of age. Some prominence of the costochondral junctions also may be physiologic in the young infant. Lateral bowing of the tibias is encountered in normal infants, and this sometimes may be quite marked in the absence of any biochemical or roentgenologic evidence of rickets. The diagnosis of rickets should not be made unless there is biochemical evidence, i e., reduction of the concentration of serum phosphorus and, less regularly, of serum calcium and an increased serum alka-

line phosphatase activity. In addition, roentgenologic evidence of a lag in calcification of the epiphyseal cartilage should be present. In the sequence of development of rickets, histologic and biochemical changes precede obvious roentgenologic evidence or clinically demonstrable skeletal deformities.

At the present time the vast majority of cases of rickets with skeletal changes of a degree which can be recognized clinically, and particularly those cases with serious deformity, are not due to nutritional vitamin D deficiency but to some endogenous metabolic defect that leads to resistance to vitamin D and lack of response to the usual amounts of vitamin D administered prophylactically. Some of the important categories of rickets on this basis are described in the following sections. All these various forms of rickets unresponsive to usual amounts of vitamin D are relatively uncommon but perhaps now no rarer than true nutritional vitamin D deficiency rickets.

FAMILIAL VITAMIN D RESISTANT RICKETS

Familial vitamin D resistant rickets is a hereditary metabolic defect in which there is failure of the normal physiologic response to vitamin D without other apparent physiologic disturbances. This defect is inherited as a dominant characteristic, so that it may be traced through successive generations as well as involve one or more siblings. A typical family tree is depicted in Figure 1, and Figure 2 shows examples of the type of bone changes seen on roentgenogram in the rachitic child and in affected adults of the family who never had been given large doses of vitamin D. However, the severity of the physiologic and the pathologic changes may be quite variable, so that the defect may not be recognized in some members of the family unless they are studied carefully. Biochemically the striking features are marked hypophosphatemia, relatively normal serum-calcium concentrations and elevated alkaline phosphatase activity in the rachitic children. Although hypocalcemia does not occur in these patients, a defect of calcium absorption is present, so that stool calcium is high and urine-calcium excretion is low. If sufficiently large doses of vitamin D are given, increased efficiency of calcium and phosphate absorption from the intestine can be produced so that serum-calcium levels and urine-calcium excretion are increased, but the serum-phosphorus levels remain abnormally low. This is in contrast with the response of the child with ordinary rickets to physiologic doses of vitamin D. In such children the serum phos-



FIG. ... cases of ... rickets of ... type. ... indicate ... three ... are ... affected ... deformi...



FIG. 2. Roentgenograms of lower extremities of one of children with resistant rickets of family diagrammed in Figure 1 in comparison with those of mother and maternal grandmother.

(Left) Child, 3 years old, active rickets. Serum Ca 9.5 mg./100 ml., serum P 2.6 mg./100 ml., serum alkaline phosphatase 19 U. *(Center)* Mother, bowing of femora and genu valgum. No obvious osteomalacia at present. Serum Ca 9.7 mg./100 ml., serum P 2.4 mg./100 ml., serum alkaline phosphatase 4.6 U. *(Right)* Maternal grandmother, bowing of femora and tibias with osteomalacia and gross disorganization of bone structure. Serum Ca 11.2 mg./100 mg., serum P 1.8 mg./100 ml., serum alkaline phosphatase 5.5 U.

phorus rises rapidly to normal levels following small doses of vitamin D, and, if a single large dose of 600,000 units of vitamin D is given, the serum phosphorus may rise to concentrations above the usual average values. Failure of the mechanism which regulates serum-phosphorus concentrations to respond to vitamin D has suggested that one of the fundamental defects in resistant rickets is impairment of renal tubular reabsorption of phosphate. Studies of renal excretion of phosphate in such patients during periods of phosphate infusion indicate that renal tubular reabsorption of phosphate is reduced The reason for the failure of vitamin D to influence renal tubular reabsorption of phosphate in this group of patients is unknown, but it is assumed that there is a specific biochemical defect in renal tubule cells.

The clinical picture is somewhat variable, depending upon the severity of the process. Retardation of growth and obvious bony deformities of rickets may not be noted until the child is between 1 and 2 years of age, or even later in some instances. Progressive skeletal changes of rickets after the first year of life in infants and children who have received some vitamin D or have been exposed to sunshine should suggest this syndrome. The author has followed from birth an infant who developed vitamin D resistant rickets. The mother had vitamin D resistant rickets with residual deformities, and the infant was the result of her first pregnancy. The mother had received vitamin D supplements during pregnancy, and at birth the infant showed no abnormalities, and serum calcium and phosphorus levels were normal. Despite the feeding of 10,000 units of vitamin D daily, hypophosphatemia, a rise in alkaline phosphate activity and early roentgenologic evidence of rickets developed by 6 months of age.

The treatment of this form of rickets consists of extremely large doses of vitamin D

line phosphatase activity. In addition, roentgenologic evidence of a lag in calcification of the epiphyseal cartilage should be present. In the sequence of development of rickets, histologic and biochemical changes precede obvious roentgenologic evidence or clinically demonstrable skeletal deformities.

At the present time the vast majority of cases of rickets with skeletal changes of a degree which can be recognized clinically, and particularly those cases with serious deformity, are not due to nutritional vitamin D deficiency but to some endogenous metabolic defect that leads to resistance to vitamin D and lack of response to the usual amounts of vitamin D administered prophylactically. Some of the important categories of rickets on this basis are described in the following sections. All these various forms of rickets unresponsive to usual amounts of vitamin D are relatively uncommon but perhaps now no rarer than true nutritional vitamin D deficiency rickets.

FAMILIAL VITAMIN D RESISTANT RICKETS

Familial vitamin D resistant rickets is a hereditary metabolic defect in which there is failure of the normal physiologic response to vitamin D without other apparent physiologic disturbances. This defect is inherited as a dominant characteristic, so that it may be traced through successive generations as well as involve one or more siblings. A typical family tree is depicted in Figure 1, and Figure 2 shows examples of the type of bone changes seen on roentgenogram in the rachitic child and in affected adults of the family who never had been given large doses of vitamin D. However, the severity of the physiologic and the pathologic changes may be quite variable, so that the defect may not be recognized in some members of the family unless they are studied carefully. Biochemically the striking features are marked hypophosphatemia, relatively normal serum-calcium concentrations and elevated alkaline phosphatase activity in the rachitic children. Although hypocalcemia does not occur in these patients, a defect of calcium absorption is present, so that stool calcium is high and urine-calcium excretion is low. If sufficiently large doses of vitamin D are given, increased efficiency of calcium and phosphate absorption from th intestine can be produced so that serum calcium levels and urine-calcium excretic are increased, but the serum-phospho levels remain abnormally low. This is contrast with the response of the child ordinary rickets to physiologic doses of min D. In such children the serum

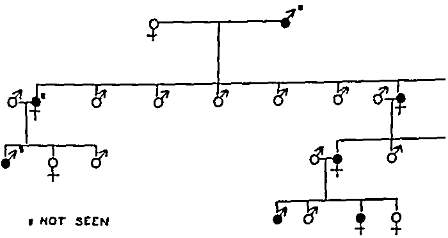


FIG 1 Family tree of cases of vitamin D resistant rickets of famil type The solid circles indicate affected individuals. Three individu are shown as probably affected on the basis of description deformities



FIG. 3. Roentgenograms of patient with clinical state resembling vitamin D resistant rickets with onset at 12 years of age. *(Left)* Distal radius and ulna on initial examination showing disorganized calcification of metaphyseal ends and generalized demineralization. Serum Ca 10.6 mg./100 ml., serum P 3.8 mg./100 ml. *(Right)* Distal radius and ulna after 12-month period of observation without treatment. No improvement noted. Serum Ca 9.6 mg./100 ml., serum P 2.8 mg./100 ml, serum alkaline phosphatase 13.8 U.

milial vitamin D resistant rickets in that the serum-calcium concentrations are in the low normal range, 9 to 10 mg. per 100 ml., while in some instances the serum-phosphorus levels are reduced to less than 2 mg. per 100 ml. Serum alkaline phosphatase activity is moderately elevated. Balance studies reveal poor intestinal absorption of calcium and reduced excretion of calcium in urine. Intestinal absorption of phosphate also is diminished, but renal clearances of phosphate are high despite the extremely low serum-phosphorus levels, indicating a defect of the renal tubular reabsorptive mechanism, which is important in the maintenance of normal serum-phosphorus levels.

The treatment of these patients is similar to that of those with familial vitamin D resistant rickets, i.e., administration of large doses of vitamin D—200,000 to 500,000 units per day. Vitamin D_2 or D_3 may be used in equivalent dosage. The problem of vitamin D toxicity is important, since these patients may develop hypercalcemia, hypercalcuria and renal injury on these dosages of vitamin D, even though the rickets and the osteomalacia may not be completely healed. Dent[8] suggests that the dose should be so regulated that the serum calcium is not increased above 11.5 mg. per 100 ml. and the urine-calcium excretion does not exceed 400 mg. per day. Striking improvement of symptoms and recalcification of bone can be achieved even though serum-phosphorus levels remain below the normal range.

Data and roentgenologic findings in a case of apparent vitamin D resistant rickets and osteomalacia beginning at adolescence are given in Figures 3 and 4. The manifestations in this boy were milder than in other cases reported, and there was symptomatic recovery following vitamin D therapy, although roentgenograms showed only partial healing. The patient has failed to return for follow-up, and the ultimate outcome is unknown.

RENAL TUBULAR ACIDOSIS WITH RICKETS AND OSTEOMALACIA

This syndrome is also probably an inborn error of renal tubule cell metabolism, al-

and doses of 50,000 to 500,000 units daily may be needed. No apparent difference in response has been found with vitamin D_2 (calciferol) or vitamin D_3 (irradiated 7-dehydrocholesterol). Interestingly enough, dihydrotachysterol (Hytakerol) in amounts of 1 mg. or more per day will also produce healing of familial vitamin D resistant rickets,[11,13] although this compound has comparatively little antirachitic potency in true vitamin D deficiency rickets. Familial vitamin D resistant rickets can be treated successfully with large doses of vitamin D, but often treatment is difficult and requires extremely close supervision of the patient, since the amounts needed are close to the toxic range. The toxic quantity of vitamin D in these subjects is not necessarily greater than in normal individuals, although they are so resistant to the physiologic effects of the vitamin. Inadequate dosage results in failure of complete healing and retardation of growth, but excessive dosage causes hypercalcemia and kidney injury which may be irreversible. Treatment is controlled by serum-calcium and urine-calcium determinations and bone x-rays. A dose of vitamin D which will produce complete healing by x-ray without raising serum-calcium levels above 12 mg. per 100 ml. or urine-calcium excretion above 200 mg. per day is the goal toward which one strives. The serum-phosphorus levels usually remain below normal with this treatment, and elevation of serum-phosphorus levels above 4 to 5 mg. per 100 ml. may be an indication of renal injury due to hypervitaminosis D. In some instances addition of phosphate to the diet[14] or the administration of sodium and potassium citrates has been tried in an effort to hasten healing without increasing the dose of vitamin D to potentially toxic levels. However, it is difficult to evaluate these expedients. Following cessation of growth and fusion of epiphyses, the vitamin D dosage can be decreased, although probably it is desirable to continue vitamin D in amounts of 25,000 to 50,000 units daily to prevent the development of osteomalacic changes in late adult life. This is particularly true of the women who go through pregnancy and lactation.

If the diagnosis is made early—and this may be facilitated by the familial story—adequate treatment with vitamin D will prevent the deformities and the stunting of growth characteristic of the untreated child. If the diagnosis is not made until the second year of life or later, significant deformities may have developed and healing is so slow that these deformities may progress. Lateral and anteroposterior bowing of the femora with genu valgum, and anterior bowing and medial torsion of the tibias, may cause serious disability. Then supracondylar osteotomy may be required for a more normal gait as well as for cosmetic reasons. Complete healing of the rickets by x-ray should be obtained before osteotomies are done. It is also important to discontinue vitamin D for several weeks prior and subsequent to osteotomy, since, if the large doses of vitamin D necessary to produce healing are continued during the period of immobilization, acute hypercalcemia and hypercalcuria may occur.

VITAMIN D RESISTANT RICKETS APPEARING AT ADOLESCENCE

Only a few instances of this rare entity have been described. In essence these patients show no metabolic defect during infancy and childhood, and growth and muscle power are normal. During adolescence or early adult life, bone and joint pains, the swelling of joints, especially the ankles, and difficulty in walking develop. Severe muscle weakness may occur, and in several cases this has been marked enough to suggest a diagnosis of progressive muscular dystrophy.[16] Generalized osteomalacia with Looser-Milkman zones and irregularity of the metaphyseal ends of the bones are seen on x-ray examination. The rachitic and the osteomalacic changes can result in extreme deformities of spine and extremities. Biochemically this syndrome is similar to fa-



FIG. 3. Roentgenograms of patient with clinical state resembling vitamin D resistant rickets with onset at 12 years of age. *(Left)* Distal radius and ulna on initial examination showing disorganized calcification of metaphyseal ends and generalized demineralization. Serum Ca 10.6 mg./100 ml., serum P 3.8 mg./100 ml. *(Right)* Distal radius and ulna after 12-month period of observation without treatment. No improvement noted Serum Ca 9.6 mg./100 ml., serum P 2.8 mg./100 ml., serum alkaline phosphatase 13.8 U.

milial vitamin D resistant rickets in that the serum-calcium concentrations are in the low normal range, 9 to 10 mg. per 100 ml., while in some instances the serum-phosphorus levels are reduced to less than 2 mg. per 100 ml. Serum alkaline phosphatase activity is moderately elevated. Balance studies reveal poor intestinal absorption of calcium and reduced excretion of calcium in urine. Intestinal absorption of phosphate also is diminished, but renal clearances of phosphate are high despite the extremely low serum-phosphorus levels, indicating a defect of the renal tubular reabsorptive mechanism, which is important in the maintenance of normal serum-phosphorus levels.

The treatment of these patients is similar to that of those with familial vitamin D resistant rickets, i.e., administration of large doses of vitamin D—200,000 to 500,000 units per day. Vitamin D_2 or D_3 may be used in equivalent dosage. The problem of vitamin D toxicity is important, since these patients may develop hypercalcemia, hypercalcuria and renal injury on these dosages of vitamin D, even though the rickets and the osteomalacia may not be completely healed. Dent[5] suggests that the dose should be so regulated that the serum calcium is not increased above 11.5 mg. per 100 ml. and the urine-calcium excretion does not exceed 400 mg. per day. Striking improvement of symptoms and recalcification of bone can be achieved even though serum-phosphorus levels remain below the normal range.

Data and roentgenologic findings in a case of apparent vitamin D resistant rickets and osteomalacia beginning at adolescence are given in Figures 3 and 4. The manifestations in this boy were milder than in other cases reported, and there was symptomatic recovery following vitamin D therapy, although roentgenograms showed only partial healing. The patient has failed to return for follow-up, and the ultimate outcome is unknown.

RENAL TUBULAR ACIDOSIS WITH RICKETS AND OSTEOMALACIA

This syndrome is also probably an inborn error of renal tubule cell metabolism, al-

though the hereditary pattern is quite different from that of vitamin D resistant rickets. Many of the cases reported have been isolated ones without familial occurrence, although there have been several examples of siblings with this lesion, suggesting the possibility of inheritance as a recessive character. The primary biochemical disturbance is the failure of excretion of an acid urine, and it is postulated that there is a defect of the mechanism whereby H^+ ions from the renal tubule cells are exchanged for Na^+, K^+, Ca^{++} and other cations in the glomerular filtrate. Since this mechanism in the normal subject is inhibited by agents that inhibit carbonic anhydrase activity, the possibility that a deficiency of carbonic anhydrase in renal tubule cells is the primary biochemical lesion has been suggested, but there is no actual proof of this. The urine of these subjects is always neutral or alkaline, and an excessive loss of bicarbonate in the urine results. On the usual acid-ash diet there is consequent depletion of extracellular bicarbonate, so that a metabolic acidosis with reduction of serum bicarbonate and elevation of serum chloride is found. The concurrence of a hyperchloremic acidosis with the excretion of a neutral or slightly alkaline urine is the characteristic finding of renal tubular acidosis. One of the important clinical manifestations of the chronic acidosis is retardation of growth. In addition, polyuria with excretion of urine of low specific gravity occurs, and this may be one of the first complaints. Although a defect of water reabsorption is found, the urine specific gravity is not fixed at as low levels as those seen in true diabetes insipidus. Impairment of renal tubular reabsorption of phosphate and consequent hypophosphatemia are associated with the chronic acidosis, and this is the basis for the bony changes of rickets and osteomalacia seen in this syndrome.

Albright has suggested that excessive loss of calcium in the urine is a primary factor and that the defect of renal tubule reabsorption of phosphate is a manifestation of hyperparathyroidism secondary to calcium deficiency, but it is possible that primary disturbance of renal tubular mechanisms is responsible. A manifestation of extreme interest is the nephrocalcinosis that may be present. The calcification in renal tubules may be sufficiently marked to be visualized by x-ray, but despite striking nephrocalcinosis in the medulla of the kidney the glomeruli are not affected, and the glomerular filtration rate can be normal. The renal calcification has been thought by Albright[1] to be due to the hypercalcuria, but another possible mechanism has been suggested by the finding that the urine of patients with renal tubular acidosis is devoid of citrate[11] although alkaline in pH. In the normal subject, urine citrate is increased if the urine is made alkaline by feeding alkalinizing salts and the citrate complexes with calcium reducing the concentration of ionized calcium. This increase of citrate in the normal subject may be of significance in preventing precipitation of calcium salts in alkaline urine, and the defect of urine-citrate excretion in renal tubular acidosis might be an important factor in the production of nephrocalcinosis.

The initial complaints usually are poor growth, polyuria and, if the process is not recognized until the end of the first year of life or later, rachitic deformities. The urine is found to have a relatively low specific gravity and is neutral or alkaline in reaction. No sugar or albumin or fixed elements are found. Renal function studies indicate normal glomerular filtration rate unless dehydration occurs. Serum analyses reveal an elevated concentration of chloride and a reduced bicarbonate level, and also low concentration of serum phosphorus with normal, or even high, levels of calcium. The blood-urea nitrogen is normal if the child is adequately hydrated. On x-ray examination demineralization of bone with rachitic changes at the metaphyses may be seen, and calcific shadows in the kidney regions are

visualized in those patients with marked renal calcinosis. Intravenous pyelograms show a relatively normal pattern.

Treatment of this syndrome is mainly correction of the metabolic acidosis, and, if the acidosis is overcome, these children do not require the very large doses of vitamin D needed for treatment of vitamin D resistant rickets. The acidosis can be treated by providing enough cation, either as sodium or sodium plus potassium, so that an alkaline urine can be excreted without depleting extracellular bicarbonate. Sodium bicarbonate, lactate or citrate can be used as a source of sodium. If molar sodium lactate solution is used, approximately 30 to 40 ml. per day is required. These patients also have been treated successfully with a solution of sodium and potassium citrate. The solution that the author has used contains 1 mM. of sodium, 1 mM. of potassium and 1 mM. of citrate per ml.* It can be made palatable by the use of a fruit-flavored syrup base, and the large amount of base required can readily be given. The citrate solutions also may have the added advantage of some antirachitic effect by virtue of keeping calcium in solution in the intestinal lumen and increasing intestinal absorption of calcium and phosphorus. Approximately 30 to 50 cc. of this solution per day, given in divided doses, has been adequate to correct the acidosis in two patients so treated. In any case, the necessary dose must be determined by serial determination of serum chloride and bicarbonate until normal levels are achieved. Improvement in well-being and appetite occurs as the acidosis is corrected, and growth is accelerated. If doses of vitamin D of approximately 5,000 to 10,000 units per day also are given, the serum phosphate returns to normal as the acidosis is corrected, but this amount of vitamin D will be relatively ineffective if the acidosis is not treated. With adequate therapy, body growth and skeletal calcification become normal. However, the underlying renal defect is not cured, and cessation of treatment results in recurrence of acidosis and hypophosphatemia. The polyuria also persists despite correction of acidosis, and urine-citrate levels remain abnormally low. Although, apparently, the renal calcinosis is not reversible, treatment may prevent or retard progression.

* Citric acid, 70 Gm.
Sodium citrate, 98 Gm.
Potassium citrate, 108 Gm.
Made up to 1 liter in fruit-flavored syrup base.



FIG. 4. Distal radius and ulna following 8 months of treatment with vitamin D, 200,000 U/day. Normal calcification of newly formed bone, although shaft of bone still is poorly mineralized. Serum Ca 10.6 mg./100 ml., serum P 4.2 mg./100 ml., serum alkaline phosphatase 8.2 U

If treatment has been started before the rachitic changes have become severe, complete healing of the rickets without deformity can be attained. However, in some instances such deformities as bowing of femora and tibias and genu valgum may become marked despite healing of the rachitic changes by x-ray, and then osteotomy may be required for correction of deformity. Figure 5 shows growth curves of

two children with renal tubular acidosis. In one case the acidosis was adequately treated, and normal growth and skeletal calcification resulted. In the other, treatment was sporadic, resulting in the stunting of growth and incompletely healed rickets.

THE FANCONI SYNDROME

This name has been applied to a group of clinical states in which the common denominator is renal glycosuria, renal amino-aciduria and hypophosphatemia with associated rickets and osteomalacia.[9] In this syndrome is found the most obvious suggestion that hypophosphatemia is the result of impaired renal tubular function, since the glycosuria and the amino-aciduria are also evidences of renal tubular dysfunction. The renal tubular injury may be the result of diverse agents, whether congenital or acquired, so that actually there are a number of distinct forms of the Fanconi syndrome.

The first of this group to be described is now termed cystine-storage disease, or Lignac-Fanconi disease.[4] This is a congenital and hereditary disorder of metabolism, and the transmission is characteristic of a recessive gene. The parents of children with this disease are normal clinically and show no biochemical disturbances by ordinary methods of examination. In the affected children, clumps of cystine crystals are found in macrophages of bone marrow, liver, spleen, lymph nodes, kidney and other tissues In addition to demonstration of cystine deposits in tissue by biopsy, cystine crystals can be found in the cornea by slit-lamp microscopy, and this is a useful diagnostic test. This cystinosis is presumably the earliest manifestation of the primary metabolic abnormality, and the evidences of renal tubular injury appear after cystine deposits in tissue are demonstrable. Infants of affected families have been followed from birth on,[3] and the renal glycosuria and amino-aciduria and the hypophosphatemia were not found until about 6 months of age and were preceded by evidences of cystine deposition in tissue. On the other hand, an anatomic abnormality of the renal tubules in this syndrome has been demonstrated by Clay, Darmady and Hawkins,[7] who suggest that there is a congenital anomaly of development of the proximal convoluted tubule.

Usually the patients are seen in the first year of life because of poor growth associated often with frequent infections. By 12 to 18 months of age clinical as well as roentgenologic evidences of rickets develop, and in the milder cases the initial complaint may be rachitic deformities of the lower extremities with awkwardness of gait. Characteristic rachitic changes are found on roentgenogram. The serum shows normal or low serum-calcium concentrations with markedly reduced serum-phosphorus levels. Blood-sugar and amino-acid levels are normal, but glucose and amino acids are found in urine in excessive amounts. The amino-aciduria is generalized with increased excretion of all the amino acids found normally in plasma. Demonstration of amino-aciduria by the paper chromatographic technic is one of the major contributions to the study of this disease. However, generalized amino-aciduria may also be found in ordinary vitamin D deficiency rickets[14] but usually quantitatively less marked than in the Fanconi syndrome. A mild metabolic acidosis has been seen in cystine-storage disease, but the urine also is acid, and by careful study this syndrome can be separated from renal tubular acidosis with rickets. The demonstration of cystine storage in tissues is, of course, pathognomonic. Excessive urine loss of potassium with low levels of serum potassium may on occasion be of importance but is not seen in all patients.

Ordinarily the clinical picture is one of progression. Although in the early stages the renal lesion is primarily tubular, diffuse scarring of the kidneys occurs in the later stages, and severe renal insufficiency may be a terminal phenomenon. In addition, hepatic cirrhosis may occur. Frequently death results from superimposed infection.

Despite the generally unfavorable course of the disease, the hypophosphatemia and the rickets can be healed by administration of vitamin D; doses of 25,000 to 50,000 units will be adequate for this purpose. In addition, the use of sodium and potassium-citrate solutions of the type used in renal tubular acidosis may also be of value, particularly in those patients with chronic acidosis and hypokalemia. Improvement of growth may follow such treatment, and reduction of the amino-aciduria and the glycosuria has been reported to occur following vitamin D and citrate therapy. However, no effect of therapy upon cystine accumulation in tissues has been noted.

The Fanconi syndrome may also be due to causes other than cystinosis. The manifestations of renal glycosuria, generalized amino-aciduria, hypophosphatemia and rickets or osteomalacia have been found in older children and adults who had no apparent disturbances of growth or bone development in infancy. In these cases with later onset of disease cystine crystals are not found in the reticulo-endothelial system.[8] In some of these patients, congenital metabolic defects may be the underlying factor, but in others it is possible that the renal tubular dysfunction is on an acquired basis. Renal amino-aciduria and glycosuria can be produced by exposure to heavy metals such as lead, cadmium, uranium and mercury,[6] and a case of Fanconi syndrome with hypophosphatemia and rickets due to lead poisoning has been reported.[5] Experimentally renal tubular dysfunction, manifested by renal glycosuria, amino-aciduria and phosphatemia, can be produced in animals by injections of maleic acid,[12] and amino-aciduria has been found in patients with a variety of metabolic disturbances with and without hypophosphatemia and disorders of calcification. However, in the cases of Fanconi syndrome reported in adults, as well as most of those seen in later childhood, no known etiologic factor has been demonstrated

Usually the presenting manifestations of this type of Fanconi syndrome are the deformities and signs of rickets and osteomalacia, despite an ordinarily adequate intake of vitamin D and calcium. Serum analysis reveals hypophosphatemia, and, on urine examination, glycosuria and amino-aciduria can be demonstrated. Treatment with moderately large doses of vitamin D, up to 50,000 units per day, usually will suffice to produce good skeletal calcification with abatement of symptoms. These patients do not show the complications of renal and hepatic insufficiency seen in cystinosis.

HYPOPHOSPHATASIA

Actually this clinical and biochemical syndrome is not properly included in the skeletal disorders resulting from hypophosphatemia, since hypophosphatemia is not necessarily observed in this entity. However, it is mentioned since the manifestations are those of a disturbance of skeletal calcification that starts in infancy and may be confused with rickets.[17,19] The bony deformities resemble those of rickets, and the roentgenogram shows marked disorganization of calcification at the metaphyseal ends of the bones. The striking biochemical finding is marked reduction of serum alkaline phosphatase activity, which is of course the reverse of what is found in the various forms of rickets. The serum-phosphorus concentrations usually are in the normal range. No consistent change in serum-calcium concentrations are found, but abnormally high levels, up to 12 to 15 mg. per 100 ml., have been recorded occasionally in such patients.

The disease probably is hereditary with lack of alkaline phosphatase in tissues as well as in serum, and deficiency of phosphatase activity in osteoblasts is considered to be the basis for failure of calcification of bone. Presumably the full-blown disease represents the homozygous state for the abnormal gene. Parents of an affected child may show an abnormally low serum alkaline phosphatase activity without bony change. Spontaneous improvement with more normal calcification of bones tends to occur as the

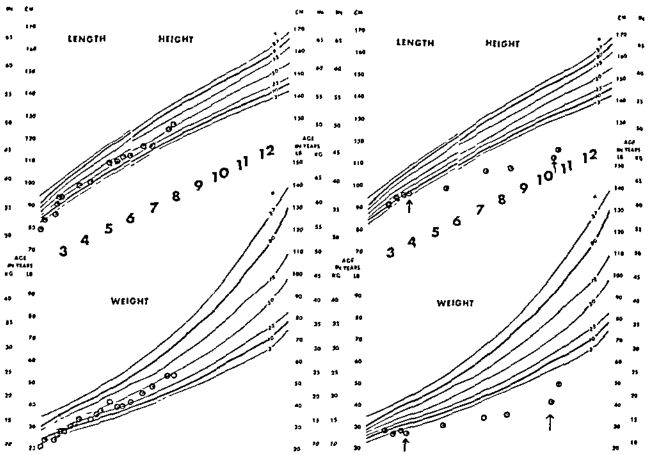


FIG. 5. Growth curves of children with renal tubular acidosis and hypophosphatemic rickets.

(Left) Diagnosis at 2 years of age with findings of hyperchloremic acidosis, florid rickets and stunting of growth. Treated with 40 ml molar sodium lactate solution and 50,000 units vitamin D daily with correction of acidosis and healing of rickets. Note resumption and maintenance of normal growth over period of 7 years with continued treatment and careful control of acidosis. No nephrocalcinosis demonstrable. No residual bony deformities.

(Right) Diagnosis at 3 months of age with findings of hyperchloremic acidosis and poor growth Initial response to treatment with sodium lactate and 5,000 units vitamin D daily. Between 3 and 4 years of age treatment was allowed to lapse (left-hand arrow), and subsequent control was poor. Growth was markedly retarded, and active rickets was present at 10 years of age. Treatment with sodium potassium citrate solution started (right-hand arrow) without change in vitamin D dosage. During next 6 months rickets healed, and suggestive spurt of growth was noted. Nephrocalcinosis present by roentgenogram, and severe deformities of lower extremities have developed in this boy.

child grows older, although alkaline phosphatase activity remains low. Premature fusion of cranial sutures has been reported as a complication of hypophosphatasia. Improved calcification of the long bones following cortisone administration also has been claimed, but in view of the tendency to spontaneous healing this must be interpreted with caution at the present time.

REFERENCES

1. Albright, F., Burnett, C. H., Parson, W., Reifenstein, E. C., Jr., and Roos, A.: Osteomalacia and late rickets: the various etiologies met in the United States with emphasis on that resulting from a special form of renal acidosis; the therapeutic indications for each etiological sub-group and the relationship between osteomalacia and Milkman's syndrome, Medicine 25:399, 1946.

2. Albright, F., and Reifenstein, E. C.: The Parathyroid Glands and Metabolic Bone Disease, Baltimore, Williams & Wilkins, 1948.
3. Bickel, H.: Die Entwickelung der biochemischen Läsion bei der Lignac-Fanconischen Krankheit, Helvet. paediat. acta 10:259, 1955.
4. Bickel, H., Smallwood, W. C., Smellie, J. M., and Hickmans, E. M.: Clinical description, factual analysis, prognosis and treatment of Lignac-Fanconi disease, Acta paediat. 42:27 (Supp. 90), 1952.
5. Chisolm, J. J., Jr., Harrison, H. C., Eberlein, W. R., and Harrison, H. E.: Amino-aciduria, hypophosphatemia, and rickets in lead poisoning; study of a case, A.M.A. Am. J. Dis. Child. 89:159, 1955.
6. Clarkson, T. W., and Kench, J. E.: Urinary excretion of amino acids by men absorbing heavy metals, Biochem. J. 62:361, 1956.
7. Clay, R. D., Darmady, E. M., and Hawkins, M.: The nature of the renal lesion in the Fanconi syndrome, J. Path. & Bact. 65: 551, 1953.
8. Dent, C. E., and Harris, H.: Hereditary forms of rickets and osteomalacia, J. Bone & Joint Surg. 38B:204, 1956.
9. Fanconi, G.: Der frühinfantile nephrotisch-glykosurische Zwergwuchs mit hypophosphatämischer Rachitis, Jahrb. f. Kinderheilk. 147:299, 1936.
10. Harrison, H. E : The disappearance of rickets: vitamin D milk as related to mineral nutrition, Quart. Rev. Pediat. 8:232, 1953.
11. ———: Mechanisms of action of vitamin D, Pediatrics 14:285, 1954.
12. Harrison, H. E., and Harrison, H. C.: Experimental production of renal glycosuria, phosphaturia and aminoaciduria by injection of maleic acid, Science 120:606, 1954.
13. ———: The renal excretion of inorganic phosphate in relation to vitamin D and parathyroid function, J. Clin. Invest. 20:47, 1941.
14. Jonxis, T. H. P., and Huisman, T. H. J.: Amino-aciduria in rachitic children, Lancet 2:428, 1953.
15. Liu, S. H., Chu, H. I., Su, C. C., Yu, T. F., and Cheng, T. Y.: Calcium and phosphorus metabolism in osteomalacia: IX. Metabolic behavior of infants fed breast milk from mothers showing various degrees of vitamin D nutrition, J. Clin. Invest. 19:327, 1940.
16. McCance, R. A.: Osteomalacia with Looser's nodes (Milkman's syndrome) due to a raised resistance to vitamin D acquired about the age of 15 years, Quart. J. Med. N.S. 16:33, 1947.
17. Rathbun, J. C.: "Hypophosphatasia"; a new developmental anomaly, A.M.A. Am. J. Dis. Child. 75:822, 1948.
18. Saville, P. D., Nassim, J. R., Harwood, F., Stevenson, K. M., and Carey, M.: The effect of A.T. 10 on calcium and phosphorus metabolism in resistant rickets, Clin. Sc. 14:489, 1955.
19. Sobel, E. H., Clark, L. C., Jr., Fox, R. P., and Robinson, M.: Rickets, deficiency of "alkaline" phosphatase activity and premature loss of teeth in childhood, Pediatrics 11:390, 1953.

Le Varietates de Rachitis e de Osteomalacia Associate con Hypophosphatemia

Summario in Interlingua

Es describite un gruppo de disordines de calcification in que hypophosphatemia es un importante defecto physiologic. Le carentia de phosphato inorganic es associate con un disbalancia inter le production del matrice ossee e le deposito de sales ossee con le resultante manifestationes pathologic e clinic de rachitis e de osteomalacia. Inefficacia del absorption de phosphato insimul con calcium ab le vias intestinal pote esser un factor significative in le genese de hypophosphatemia, sed etiam importante es le disturbation del functiones del tubulos renal quanto al reabsorption de phosphato jam filterate per le glomerulos. Rachitis hypophosphatemic, per consequente, pote esser le resultato de disordines primari in le functiones del tubulos renal.

Rachitis e osteomalacia causate per un carentia dietari de vitamina D se incontra rarmente in nostre dies. Sed carentia de vitamina D in consequentia de steatorrhea e

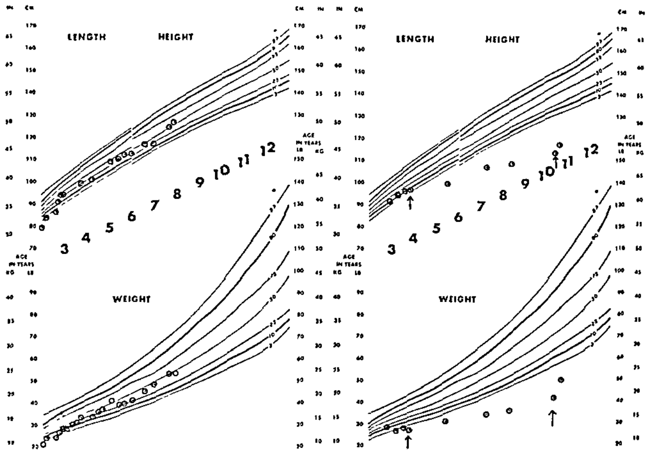


FIG. 5. Growth curves of children with renal tubular acidosis and hypophosphatemic rickets.

(Left) Diagnosis at 2 years of age with findings of hyperchloremic acidosis, florid rickets and stunting of growth. Treated with 40 ml. molar sodium lactate solution and 50,000 units vitamin D daily with correction of acidosis and healing of rickets Note resumption and maintenance of normal growth over period of 7 years with continued treatment and careful control of acidosis No nephrocalcinosis demonstrable. No residual bony deformities.

(Right) Diagnosis at 3 months of age with findings of hyperchloremic acidosis and poor growth. Initial response to treatment with sodium lactate and 5,000 units vitamin D daily. Between 3 and 4 years of age treatment was allowed to lapse (left-hand arrow), and subsequent control was poor. Growth was markedly retarded, and active rickets was present at 10 years of age. Treatment with sodium potassium citrate solution started (right-hand arrow) without change in vitamin D dosage. During next 6 months rickets healed, and suggestive spurt of growth was noted. Nephrocalcinosis present by roentgenogram, and severe deformities of lower extremities have developed in this boy.

child grows older, although alkaline phosphatase activity remains low. Premature fusion of cranial sutures has been reported as a complication of hypophosphatasia. Improved calcification of the long bones following cortisone administration also has been claimed, but in view of the tendency to spontaneous healing this must be interpreted with caution at the present time.

REFERENCES

1. Albright, F., Burnett, C. H., Parson, W., Reifenstein, E. C., Jr., and Roos, A.: Osteomalacia and late rickets: the various etiologies met in the United States with emphasis on that resulting from a special form of renal acidosis; the therapeutic indications for each etiological sub-group and the relationship between osteomalacia and Milkman's syndrome. Medicine 25:399, 1946.

7

Anabolic Steroid Therapy for the Protein Depletion and Osteoporosis Induced Corticoid Hormones*

EDWARD C. REIFENSTEIN, JR., M.D.

Corticoid materials (adrenocorticotropic hormone [ACTH], hydrocortisone [Cortisol], cortisone and related steroids with glucocorticoid activity) have dramatic beneficial effects in patients with a variety of conditions. Frequently these agents also have adverse effects upon protein and osseous tissues. The purpose of this discussion is to review these unfavorable effects and some of the evidence supporting the use of anabolic steroid therapy to control them.

THE EFFECTS OF CORTICOID HORMONES

In Cushing's syndrome, in which an excess of cortical hormones is present because of endogenous disturbances in adrenal cortical function,[1,5,45] evidences of these unfavorable effects include a thin red skin with purplish striae, easy bruisability, weakness, marked muscular wasting and relaxation of the abdominal wall;[1,5,45] a negative nitrogen balance in metabolic studies;[1,5,45,70] hypercalcuria;[26,40] and osteoporosis (atrophy of bone from inadequate protein matrix formation)[26,40] Osteoporosis is one of the most common serious manifestations of Cushing's syndrome, being present in about 90 per cent of cases.[26,40]

In nonendocrine disorders (rheumatoid arthritis, asthma, pemphigus, lupus erythematosus and similar conditions), in which an excess of cortical hormones is present because of chronic corticoid therapy, the same adverse effects have been observed on protein and osseous tissues: thin skin, easy bruisability, weakness, muscular wasting, hypercalcuria and ostéoporosis.[4,11,14-17,19,21,22,27,28,40,46,54,58,66,68-72,77,78,80,82,84] A partial survey of recorded cases on chronic corticoid therapy revealed 38 patients who developed spontaneous fractures while on medication.[63] These fractures usually involved vertebrae and occurred in 20 adults after an average of 37 Gm. (range 3.4 to 88.2 Gm.) of corticoid materials administered over an average of 471 days (range 34 to 1,148 days). In 6 children the fractures appeared after an average of 17 Gm. (range 4.9 to 47.5 Gm.) of therapy during an average of 218 days (range 71 to 478 days). The data on those individuals whose ages were recorded (17 adults and 6 children) are given in the table on page 76 which is compiled from a detailed analysis published elsewhere.[63] The spontaneous fractures following corticoid therapy are particularly frequent in (1) patients with pre-existing osteoporosis, (2) persons of middle and advanced age, (3) postmenopausal women, (4) children, (5) individuals with marked restriction of physical activity or enforced bed rest, and (6) patients who are given corticoid materials in

* From the Medical Division, The Squibb Institute for Medical Research, E. R. Squibb & Sons Division, Olin Mathieson Chemical Corporation, New York; and the Department of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals, New York, New York

non-absorption de vitamina D es un occurrentia possibile.

Le majoritate del casos de rachitis e osteomalacia nunc diagnosticate es le effecto de endogene defectos metabolic que resulta in le absentia del responsa normal a quantitates physiologic de vitamina D. Le plus commun de iste innate errores del metabolismo es Familial Rachitis Resistente a Vitamina D. Isto es un disordine hereditari que se *transmitte* como *dominante mendelian.* Il occurre grande variationes in le severitate del processo de maniera que sever formas de rachitis e arresto de crescentia se incontra in certe juveniles durante que altere patientes manifesta solmente moderate retardation del crescentia con leve alterationes osteomalacic. Le tractamento require grande *doses de vitamina D, a vices proxime al* limine de toxicitate. Es etiam describite un disordine simile a Familial Rachitis Resistente a Vitamina D sed sin historia de incidentia familial e con declaration al adolescentia.

Acidosis reno-tubular con hypophosphatemia e rachitis es etiam un defecto congenite *ben que le schema del transmission* hereditari es obscur. Acidosis hyperchloremic e polyuria con crescentia atrophic es constatationes importante. Le tractamento del acidosis con citrato de natrium e kalium o altere fontes de un excesso de cationes pote resultar in un curation symptomatic *ben que le* subjacente defecto tubular non es eliminate.

Le syndrome de Fanconi representa un constellation de glycosuria renal, aminoaciduria renal, phosphaturia renal, e hypophosphatemic rachitis o osteomalacia. Isto pote esser le resultato de un hereditari disordine metabolic associate con deposition de cystina *in le histos* (declarate in le infantia del patiente) o de un insulto del tubulos renal de origine incognite (occurrente plus tarde in le vita). Le forma familial del syndrome de Fanconi, debite a dysfunction del immagasinage de cystina, es transmittite como recessivo mendelian. Le occurrentias sporadic de syndrome de Fanconi sin cystinosis, que es *incontrate in* individuos de etates plus avantiate, exhibi nulle tendentia familial. Le differentiation e le tractamento de iste conditiones es discutite.

Assi il es nunc possibile separar un numero de disordines de calcification associate con defecto del function del tubulos *renal e con hypophosphatemia. Le modo de* tractamento e le prognose differe in le differente disordines. Isto explica le importantia del differentiation inter iste varie formas de rachitis e osteomalacia.

coming the deleterious effects through a favorable action in the opposite direction (see Fig. 1).

CONDITIONS WITH AN EXCESS OF CORTICOID HORMONES

An absolute excess of endogenous corticoid hormones over anabolic steroids occurs in Cushing's syndrome;[1,5,45] and a relative excess of endogenous corticoid hormones over anabolic steroids occurs in the normal child,[30,73,76] in older persons,[3,13,30,35,36,76] in the postmenopausal state[3,13,30,35,36,76] and in hypogonadism associated with normal

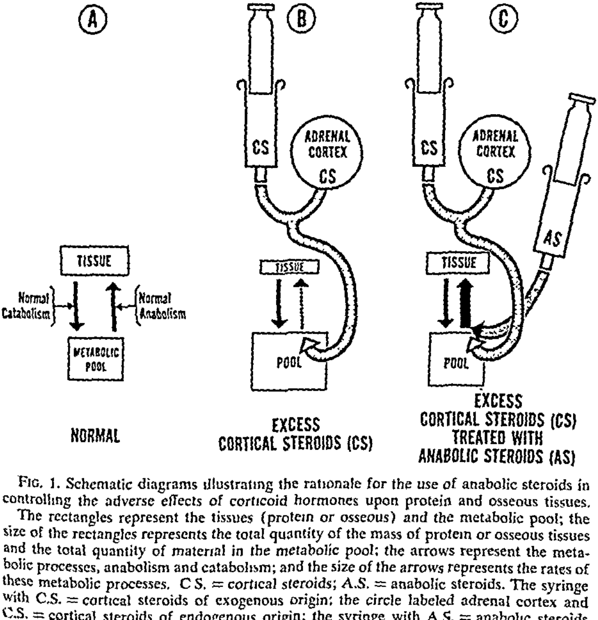


FIG. 1. Schematic diagrams illustrating the rationale for the use of anabolic steroids in controlling the adverse effects of corticoid hormones upon protein and osseous tissues.

The rectangles represent the tissues (protein or osseous) and the metabolic pool; the size of the rectangles represents the total quantity of the mass of protein or osseous tissues and the total quantity of material in the metabolic pool; the arrows represent the metabolic processes, anabolism and catabolism; and the size of the arrows represents the rates of these metabolic processes. C.S. = cortical steroids; A.S. = anabolic steroids. The syringe with C.S. = cortical steroids of exogenous origin; the circle labeled adrenal cortex and C.S. = cortical steroids of endogenous origin; the syringe with A.S. = anabolic steroids of exogenous origin.

The diagram has 3 divisions: (A) the normal total mass of protein or osseous tissues that results from the dynamic equilibrium between these tissues and the metabolic pool when the rates of anabolism and catabolism are both normal, (B) the decreased total mass of protein or osseous tissues that results when the rate of anabolism is decreased by the antianabolic effect of excess cortical steroids of endogenous or exogenous origin (in this division the rate of catabolism is normal); and (C) the partially restored total mass of protein or osseous tissues that results when the antianabolic effect of the excess cortical hormones on the rate of anabolism is offset by the stimulating effect of anabolic steroids of exogenous origin on the rate of anabolism (in this division the rate of catabolism is normal). (Reifenstein, E. C., Jr., South. M. J. 49:933-960)

large amounts and/or for prolonged periods. In one study, two thirds of 21 asthmatic patients on chronic corticoid medication developed hypercalcuria, and one had spontaneous fractures.[40] Negative nitrogen and phosphorus balances have been induced by corticoid hormones in human metabolic studies.[8,29,45,52,59,70,71] In animals, corticoid materials may have adverse effects upon protein tissues and growth.[10,18,39,67,83] It is believed[63] that these unfavorable manifestations of corticoid hormones are the result of an antianabolic rather than a catabolic effect *upon protein and osseous tissues.*

THE EFFECTS OF GONADAL HORMONES

The gonadal hormones androgen and estrogen have a stimulating effect upon the growth of protein and osseous tissues. This favorable action is manifested by marked growth in height, weight, musculature, strength and bone in male patients with excessive amounts of endogenous androgen arising from Leydig cell tumors of the testis;[43,75,86] occasionally by rapid acceleration of skeletal growth and excessive somatic development in female patients with abnormally increased amounts of endogenous estrogen arising from granulosa cell tumors of the ovary;[74,81,86] by *somatic alterations* with an increase in musculature, weight and mature bone in hypogonad male individuals whose endogenous androgen production has been accelerated by the administration of chorionic gonadotropin;[23,42,53] and by an increase in muscle mass, weight, height and bone maturation in eunuchoid males treated with potent androgenic compounds,[41,42,55] *and in sexually underdeveloped females* treated with potent estrogenic hormones.[32,79] Positive balances of nitrogen and other constituents of protein (in the proper proportions for protein tissues)[42-44,50,51,64,87] and of calcium and phosphorus (in the proper proportions for osseous tissues)[9,33,65] have been induced in human metabolic balance studies with androgens[42,43,50,64] and estrogens[50,64] Testosterone *compounds have a greater* effect upon protein structures, estradiol steroids have a greater effect upon bone, and the combination of androgens and estrogens has the most marked effect upon osseous tissues.[2,3,64,65] These anabolic responses to steroids occur regardless of the state of the endocrine glands,[62] and even in patients on an inadequate protein and caloric intake who are utilizing tissue proteins for energy.[7,48,49] In animals, the anabolic effects of androgens and/or estrogens have been demonstrated in many species.[51] It is believed[63] that these *stimulating effects of gonadal hormones* are the result of an anabolic rather than an anticatabolic effect upon protein and osseous tissues.

THE EFFECTS OF ANABOLIC GONADAL STEROIDS IN COMBINATION WITH CORTICOID HORMONES

When anabolic gonadal steroids are administered simultaneously with corticoid materials, the adverse effects of the latter are prevented or minimized if suitable doses are employed. The favorable effect of such anabolic therapy is attested by the improvement in the clinical manifestations of Cushing's syndrome following the administration of androgens[1-3,5,6,12,20,34,38,45,47,61,61,70,85] or estrogens;[6,24,25,31,57,59-61,64] by the induction of positive balances of protein and osseous tissue constituents with these hormones alone and in combination in Cushing's syndrome;[1-3,5,6,20,56,59,64,65,70,71,77] by the induction of similar positive balances with anabolic steroids in patients receiving chronic corticoid therapy;[8,58] and by the elimination of *corticoid-therapy-induced* hypercalcuria with simultaneous anabolic steroid medication.[16,40] The evidence indicates that the simultaneous administration of anabolic hormones does not interfere with the beneficial effects of the corticoid materials upon the underlying disease.[8,16,27,37,40,68-72,79] It is believed[73] that the anabolic steroids counteract the adverse effects of the corticoid hormones by over-

tomy is the main therapeutic procedure for persistent and/or severe Cushing's syndrome, anabolic steroids are indicated preoperatively to protect the tissues from further depletion and to initiate the restorative processes; after operation, such patients should be placed upon anabolic steroid therapy at least until the adverse effects upon protein and osseous tissues are eliminated. It should be noted that in those patients with Cushing's syndrome resulting from a malignant adrenal cortical tumor, anabolic steroids are not recommended, since they may stimulate the growth of the neoplastic lesion.

Furthermore, the evidence indicates that anabolic steroids should be administered *to prevent* the adverse effects upon protein and osseous tissues in patients who are being started on a regimen of chronic corticoid medication. The anabolic steroids should be given for the entire period that the corticoid materials are being taken. Finally, the evidence summarized above provides strong support for the contention that to prevent the development of protein depletion and osteoporosis, anabolic steroids should be administered to all persons who have passed the prime of life and are becoming elderly, to all women at and after the time of the menopause, and to patients with hypogonadism and normal adrenal cortical function. The preventive use of anabolic steroids is indicated in those patients on minimal replacement doses of corticoid agents for adrenal cortical insufficiency who in addition have gonadal insufficiency. These individuals lack sufficient endogenous anabolic steroids to offset the adverse effects of corticoid hormones even when the level of the corticoid substances is within the normal range.

At present the combination of androgen with estrogen provides the most potent and practical anabolic preparation that is available for therapy. Such a combination has the advantage (1) of adding the more marked osseous-anabolic effect of the estrogen to the more marked protein-anabolic effect of the androgen and (2) of reducing the incidence of undesirable responses (of the single-hormone type) in the genital organs and the accessory sexual structures. The preparation recently introduced as Deladumone* (90 mg. of testosterone enanthate and 4 mg. of estradiol valerate dissolved in each milliliter [cc.] of sesame oil) seems to meet the requirements very satisfactorily. The usual dosage for anabolic therapy is 1 to 2 milliliters (cc.);

* Made by E. R. Squibb & Sons Division, Olin Mathieson Chemical Corporation, New York, N. Y.

AMOUNT AND DURATION OF CORTICOID THERAPY BEFORE THE ONSET OF SPONTANEOUS FRACTURES IN CHILDREN AND ADULTS OF BOTH SEXES

TYPE OF PATIENT	NUMBER OF PATIENTS	AGE, AVERAGE AND RANGE (YEARS)	TOTAL THERAPY* BEFORE FRACTURE: AVERAGE AND RANGE (GM.)	DURATION OF THERAPY BEFORE FRACTURE: AVERAGE AND RANGE (DAYS)
Girls	2	4.5 (3-6)	5.3 (4.9-5.72)	97 (76-119)
Boys	4	8.5 (3-11)	22.8 (7.09-47.5)	279 (71-478)
Women	9	56.2 (45-70)	30.5 (3.4-72.9)	352 (34-865)
Men	8	61.1 (48-72)	42.7 (7.3-88.2)	605 (73-1148)

* Cortisone plus hydrocortisone plus adrenocorticotropic hormone (ACTH)

adrenal cortical function.[63] An excess of administered corticoid hormones over endogenous anabolic steroids occurs with the administration of these hormones in large amounts and/or for prolonged periods.[63] The balance between the anabolic and the antianabolic steroids in various physiologic and pathologic states is shown in schematic diagrams in Figure 2.

INDICATIONS FOR THERAPY WITH ANABOLIC STEROIDS

The evidence reviewed above indicates that anabolic steroids should be administered *to restore* the protein and the osseous tissues in patients who have protein depletion and/or osteoporosis associated with Cushing's syndrome from benign lesions, old age, the postmenopausal state, hypogonadism with normal adrenal cortical function, and chronic corticoid therapy. The administration of anabolic steroid therapy should be continued until the depletion of protein and osseous tissues has been corrected and the excess of corticoid hormones has been eliminated. Therefore, in all patients with protein depletion and/or osteoporosis associated with old age, with the postmenopausal state and with hypogonadism and normal adrenal corticoid function, treatment will be needed through the balance of life. In patients who are receiving chronic corticoid medication, the administration of anabolic steroid therapy should be continued until the depletion of tissues is eliminated and/or the corticoid medication is stopped. Although adrenalec-

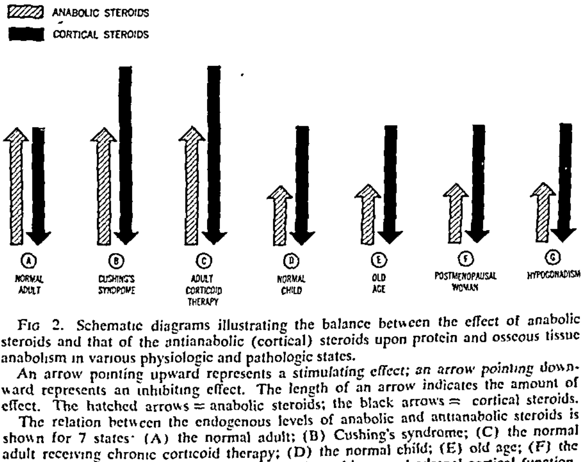


FIG 2. Schematic diagrams illustrating the balance between the effect of anabolic steroids and that of the antianabolic (cortical) steroids upon protein and osseous tissue anabolism in various physiologic and pathologic states.

An arrow pointing upward represents a stimulating effect; an arrow pointing downward represents an inhibiting effect. The length of an arrow indicates the amount of effect. The hatched arrows = anabolic steroids; the black arrows = cortical steroids.

The relation between the endogenous levels of anabolic and antianabolic steroids is shown for 7 states: (A) the normal adult; (B) Cushing's syndrome; (C) the normal adult receiving chronic corticoid therapy; (D) the normal child; (E) old age; (F) the postmenopausal woman; and (G) hypogonadism with normal adrenal cortical function.

It will be seen that there is a balance between the hormonal influences in the normal adult (A), that there is an absolute increase in the antianabolic action in Cushing's syndrome and in the normal adult receiving chronic corticoid therapy (B & C), and that there is a relative increase in the antianabolic action (as a result of a decrease in the anabolic action) in the normal child, in old age, in the postmenopausal woman, and in hypogonadism with normal adrenal corticoid function (D, E, F & G). (Reifenstein, E. C., Jr., South M J 49:933-960)

adrenal cortical function.[63] An excess of administered corticoid hormones over endogenous anabolic steroids occurs with the administration of these hormones in large amounts and/or for prolonged periods.[63] The balance between the anabolic and the antianabolic steroids in various physiologic and pathologic states is shown in schematic diagrams in Figure 2.

INDICATIONS FOR THERAPY WITH ANABOLIC STEROIDS

The evidence reviewed above indicates that anabolic steroids should be administered *to restore* the protein and the osseous tissues in patients who have protein depletion and/or osteoporosis associated with Cushing's syndrome from benign lesions, old age, the postmenopausal state, hypogonadism with normal adrenal cortical function, and chronic corticoid therapy. The administration of anabolic steroid therapy should be continued until the depletion of protein and osseous tissues has been corrected and the excess of corticoid hormones has been eliminated. Therefore, in all patients with protein depletion and/or osteoporosis associated with old age, with the postmenopausal state and with hypogonadism and normal adrenal corticoid function, treatment will be needed through the balance of life. In patients who are receiving chronic corticoid medication, the administration of anabolic steroid therapy should be continued until the depletion of tissues is eliminated and/or the corticoid medication is stopped. Although adrenalec-

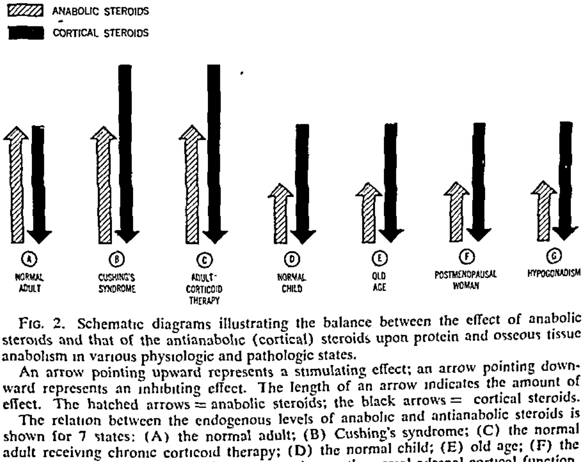


FIG. 2. Schematic diagrams illustrating the balance between the effect of anabolic steroids and that of the antianabolic (cortical) steroids upon protein and osseous tissue anabolism in various physiologic and pathologic states.

An arrow pointing upward represents a stimulating effect; an arrow pointing downward represents an inhibiting effect. The length of an arrow indicates the amount of effect. The hatched arrows = anabolic steroids; the black arrows = cortical steroids.

The relation between the endogenous levels of anabolic and antianabolic steroids is shown for 7 states: (A) the normal adult; (B) Cushing's syndrome; (C) the normal adult receiving chronic corticoid therapy; (D) the normal child; (E) old age; (F) the postmenopausal woman, and (G) hypogonadism with normal adrenal cortical function.

It will be seen that there is a balance between the hormonal influences in the normal adult (A), that there is an absolute increase in the antianabolic action in Cushing's syndrome and in the normal adult receiving chronic corticoid therapy (B & C), and that there is a relative increase in the antianabolic action (as a result of a decrease in the anabolic action) in the normal child, in old age, in the postmenopausal woman, and in hypogonadism with normal adrenal corticoid function (D, E, F & G). (Reifenstein, E. C., Jr: South M J. 49:933-960)

tomy is the main therapeutic procedure for persistent and/or severe Cushing's syndrome, anabolic steroids are indicated preoperatively to protect the tissues from further depletion and to initiate the restorative processes; after operation, such patients should be placed upon anabolic steroid therapy at least until the adverse effects upon protein and osseous tissues are eliminated. It should be noted that in those patients with Cushing's syndrome resulting from a malignant adrenal cortical tumor, anabolic steroids are not recommended, since they may stimulate the growth of the neoplastic lesion.

Furthermore, the evidence indicates that anabolic steroids should be administered to *prevent* the adverse effects upon protein and osseous tissues in patients who are being started on a regimen of chronic corticoid medication. The anabolic steroids should be given for the entire period that the corticoid materials are being taken. Finally, the evidence summarized above provides strong support for the contention that to prevent the development of protein depletion and osteoporosis, anabolic steroids should be administered to all persons who have passed the prime of life and are becoming elderly, to all women at and after the time of the menopause, and to patients with hypogonadism and normal adrenal cortical function.

The preventive use of anabolic steroids is indicated in those patients on minimal replacement doses of corticoid agents for adrenal cortical insufficiency who in addition have gonadal insufficiency. These individuals lack sufficient endogenous anabolic steroids to offset the adverse effects of corticoid hormones even when the level of the corticoid substances is within the normal range.

At present the combination of androgen with estrogen provides the most potent and practical anabolic preparation that is available for therapy. Such a combination has the advantage (1) of adding the more marked osseous-anabolic effect of the estrogen to the more marked protein-anabolic effect of the androgen and (2) of reducing the incidence of undesirable responses (of the single-hormone type) in the genital organs and the accessory sexual structures. The preparation recently introduced as Deladumone* (90 mg. of testosterone enanthate and 4 mg. of estradiol valerate dissolved in each milliliter [cc.] of sesame oil) seems to meet the requirements very satisfactorily. The usual dosage for anabolic therapy is 1 to 2 milliliters (cc.);

* Made by E. R. Squibb & Sons Division, Olin Mathieson Chemical Corporation, New York, N. Y.

AMOUNT AND DURATION OF CORTICOID THERAPY BEFORE THE ONSET OF SPONTANEOUS FRACTURES IN CHILDREN AND ADULTS OF BOTH SEXES

Type of Patient	Number of Patients	Age, Average and Range (Years)	Total Therapy* Before Fracture: Average and Range (Gm.)	Duration of Therapy Before Fracture: Average and Range (Days)
Girls	2	4.5 (3-6)	5.3 (4.9-5.72)	97 (76-119)
Boys	4	8 5 (3-11)	22.8 (7.09-47.5)	279 (71-478)
Women	9	56 2 (45-70)	30.5 (3.4-72.9)	352 (34-865)
Men	8	61.1 (48-72)	42.7 (7.3-88.2)	605 (73-1148)

* Cortisone plus hydrocortisone plus adrenocorticotropic hormone (ACTH)

a single intramuscular injection of this amount has a potent anabolic effect which is sustained for 3 to 4 weeks. Furthermore, the preparation appears to have an optimal androgen-to-estrogen ratio; consequently, only a very small percentage of patients of either sex respond to it with undesirable masculinizing or feminizing manifestations.

The adequacy of the anabolic steroid dosage *as corrective therapy* for protein depletion and/or osteoporosis in patients who also are receiving chronic corticoid medication can be determined in most cases by examining the urine repeatedly for hypercalcuria (which indicates an adverse corticoid hormone action upon bone). A rough estimate of the calcium content of the urine can be obtained by the use of the Sulkowich Test. The amount of anabolic compounds administered should be increased until the urinary calcium excretion falls to the normal range. The urinary calcium level should be maintained in this range throughout the corticoid regimen by adjusting the anabolic steroid dosage from time to time. When anabolic steroids are employed *as preventive therapy,* the dosage should be adjusted to maintain the patient in an optimal clinical state. Prolonged treatment is required, since the underlying endogenous imbalance between anabolic and antianabolic steroids continues to be present whenever the anabolic steroid therapy is omitted.

SUMMARY AND CONCLUSIONS

1. Anabolic steroid therapy in adequate amounts for sufficient time is indicated *to restore* the protein and the osseous tissues in patients who have protein depletion and/or osteoporosis associated with Cushing's syndrome from benign lesions, with old age, with the postmenopausal state, with hypogonadism and normal adrenal cortical function, and with prolonged and/or intensive corticoid therapy.

2 Anabolic steroid therapy in adequate amounts for sufficient time is indicated *to prevent* adverse effects upon protein and osseus tissues: (a) in patients who are being started on a regimen of chronic corticoid medication; and (b) in persons who are becoming elderly, in women at and after the menopause, and in patients with hypogonadism and normal adrenal cortical function.

3. In patients who are receiving chronic corticoid therapy, the anabolic steroid dosage should be maintained at an amount which is sufficient to prevent hypercalcuria (which indicates an adverse effect of corticoid hormone upon bone).

4. The combination of androgen with estrogen appears to be the most potent and the most practical anabolic preparation now available for either the treatment or the prevention of the adverse effects of corticoid hormones upon the protein and the osseous tissues.

REFERENCES

1. Albright, F.: Cushing's syndrome: its pathological physiology, its relationship to the adreno-genital syndrome, and its connection with the problem of the reaction of the body to injurious agents ("alarm reaction" of Selye). Harvey Lect. 38:123-186, 1942-1943.
2. ———: Effect of hormones on osteogenesis in man, Rec. Progr. Hormone Res. 1: 293-353, 1947.
3. ———: Osteoporosis, Ann. Int. Med. 27: 861-882, 1947.
4. Albright, F., and Henneman, P. H.: Osteoporosis produced by cortisone-like steroids *in* Tr. Conf. on Metabolic Interrelations, *with Special Reference to Calcium,* vol. 5, pp. 191-195, New York, Macy, 1953.
5. Albright, F., Parson, W., and Bloomberg, E.: Cushing's syndrome interpreted as hyperadrenocorticism leading to hypergluconeogenesis: results of treatment with testosterone propionate, J. Clin. Endocrinol. 1:375-384, 1941.
6. Albright, F., and Reifenstein, E. C., Jr.: Ch. 6: Metabolic bone disease: Osteoporosis, II. Clinical aspects of osteoporosis, (F) Osteoporosis of Cushing's syndrome, *in* The Parathyroid Glands and Metabolic Bone Disease: Selected Studies, pp. 165-181, Baltimore, Williams & Wilkins, 1948.

7. Albright, F., Reifenstein, E. C., Jr., and Forbes, A. P.: Changes induced by testosterone propionate in a very obese individual on a very low nitrogen and low caloric intake *in* Tr. Conf. on Metabolic Aspects of Convalescence, Including Bone and Wound Healing, vol. 5, pp. 74-77, New York, Macy, 1943.
8. Bartter, F. C., Fourman, P., Albright, F., Jefferies, W. McK., Dempsey, E., and Carroll, E. L.: Does methyl testosterone modify the effects of adrenocorticotropic hormone (ACTH) and of desoxycorticosterone glucoside (DOCG)? *in* Christman, R. C. (ed.): Pituitary-Adrenal Function, pp. 109-121, Tr. Symp. Section M. Sc. of Am. A. Adv. Sc., Washington, D. C., Am. A. Adv. Sci., 1951.
9. Bassett, S. H., Keutmann, E. H., and Kochakian, C. D.: Comparative effects of methyl androstanediol orally and testosterone propionate intramuscularly *in* Tr. Conf. on Metabolic Aspects of Convalescence, Including Bone and Wound Healing, vol. 6, pp. 75-79, New York, Macy, 1944.
10. Becks, H., Simpson, M. E., Li, O. H., and Evans, H. M.: Effects of adrenocorticotrophic hormone (ACTH) on the osseous system in normal rats, Endocrinology 34: 305-310, 1944.
11. Berrios de la Luz, R., and Eulufi Marin, R.: Rheumatoid arthritis and Cushing's syndrome consecutive to prolonged use of cortisone; clinical case, Rev. méd Chile 81:565-568, 1953.
12. Bishop, P. M. F., De Mowbray, R. R., Glover, F. N., and Thorne, M. G.: The treatment of Cushing's syndrome, Lancet 267:1137-1140, 1954
13. Bliss, E. A., Sandberg, A. A., Nelson, D. H., and Eik-Nes, K: The normal levels of 17-hydroxycorticosteroids in the peripheral blood of man, J. Clin Invest. 32:818-823, 1953
14. Boland, E. W., and Headley, N. E.: Management of rheumatoid arthritis with smaller (maintenance) doses of cortisone acetate, J.A M.A 144:365-372, 1950.
15. Bunim, J. J, Ziff, N., and McEwen, C.: Evaluation of prolonged cortisone therapy in rheumatoid arthritis; a four-year study, Am. J Med. 18:27-40, 1955.
16. Burrage, W. S., Ritchie, A. C., Mansmann, H. C., Jr., Irwin, J W, and Russfield, A. B: The use of cortisone and hydrocortisone in allergy, Ann Int Med 43:1001-1018, 1955.
17. Case Records of the Massachusetts General Hospital: Case 39221, New England J. Med. 248:943-950, 1953.
18. Clark, I.: The effect of cortisone upon protein synthesis, J. Biol. Chem. 200:69-76, 1953.
19. Curtiss, F. H., Jr., Clark, W. S., and Herndon, C. H.: Vertebral fractures resulting from prolonged cortisone and corticotropin therapy, J.A.M.A. 156:467-469, 1954.
20. Deakins, M. L., Friedgood, H. B., and Ferrebee, J. W.: Some effects of testosterone, testosterone propionate, methyl testosterone, stilbestrol, and x-ray therapy in a patient with Cushing's syndrome, J. Clin. Endocrinol. 4:376-384, 1944.
21. Demartini, F., Grokoest, A. W., and Ragan, C.: Pathological fractures in patients with rheumatoid arthritis treated with cortisone, J.A.M.A. 149:750-752, 1952.
22. de Sèze, S., Hubalt, A., and Renier, J. C.: Four cases of spontaneous fractures observed in disorders treated with cortisone, Presse méd. 39:819, 1953.
23. Dorff, G. B., and Hudson, I. M.: Linear growth responses of boys to prolonged treatment with chorionic gonadotropin, J. Clin. Endocrinol. 11:343-359, 1951.
24. Dunn, C. W.: The Cushing syndrome, Endocrinology 22:374-385, 1938.
25. ———: Oestrin in the treatment of Cushing's syndrome, Lancet 233:344-345 and 828-829, 1937.
26. Eisenhardt, L., and Thompson, K. W.: Brief consideration of the present status of so-called pituitary basophilism, with tabulation of verified cases, Yale J. Biol. & Med 11:507-522, 1939.
27. Eisenstadt, W. S., and Cohen, E. S.: Osteoporosis and compression fractures from prolonged cortisone and corticotropin therapy, Ann. Allergy 13:252-256, 1955.
28. Engleman, E. P., Krupp, M. A., Saunders, W. W., Wilson, L. E., and Fredell, E. W.: Rheumatoid arthritis: an evaluation of long-term treatment with cortisone, California Med. 80:369-374, 1954.
29. Fourman, P., Bartter, F. C., Albright, F., Dempsey, E., Carroll, E., and Alexander, J.: Effects of 17-hydroxy-corticosterone ("compound F") in man, J. Clin. Invest. 29:1462-1473, 1950.
30. Fraser, R. W., Forbes, A. P., Albright, F., Sulkowitch, H., and Reifenstein, E. C., Jr.: Colorimetric assay of 17-ketosteroids in

urine: a survey of the use of this test in endocrine investigation, diagnosis and therapy, J. Clin. Endocrinol. 1:234-256, 1941.

31. Gill, A. M.: Treatment of Cushing's syndrome with large doses of oestrin, Lancet 233:70-72, 1937.
32. Goldzieher, M. A.: Growth and sex hormones, J. Clin. Endocrinol. 1:924-927, 1941.
33. Gordan, G. S.: Evaluation and use of anabolic steroids, GP 10:87-102, 1954.
34. Greenlee, R. G.: Hyperfunction of the adrenal cortex, M. Clin. North America 39:1081-1099, 1955.
35. Hamburger, C.: Normal urinary excretion of neutral 17-ketosteroids with special reference to age and sex variations, Acta endocrinol. 1:19-37, 1948.
36. Hamilton, H. B., and Hamilton, J. B.: Ageing in apparently normal men: I. Urinary titers of ketosteroids and of alpha-hydroxy and beta-hydroxy ketosteroids, J. Clin. Endocrinol. 8:433-452, 1948.
37. Henneman, P. H., Irwin, J. W., Wang, D. M. K., and Burrage, W. S: The effect of estrogen and androgen on calcium metabolism during cortisone administration, J. Clin. Endocrinol. 15:858, 1955.
38. Hubble, D.: Cushing's syndrome and thymic carcinoma, Quart. J. Med 18:133-147, 1949.
39. Ingle, D. J: Some studies on the role of the adrenal cortex in organic metabolism, Ann. New York Acad. Sc. 50:576-595, 1949.
40. Irwin, J. W., Henneman, P. H., Wang, D. M. K., and Burrage, W. S.: Maintenance cortisone in intractable asthma: preliminary observations of undesirable cortisone effects, J. Allergy 25:201-209, 1954.
41. Kenyon, A T.: The effect of testosterone propionate on the genitalia, prostate, secondary sex characters, and body weight in eunuchoidism, Endocrinology 23:121-134, 1938.
42. Kenyon, A T., Knowlton, K., Lotwin, G., Munson, P. L, Johnston, C. D., and Koch, F. C Comparison of the metabolic effects of testosterone propionate with those of chorionic gonadotropin, J. Clin. Endocrinol. 2:685-689, 1942.
43. Kenyon, A. T., Knowlton, K., and Sandiford, I The anabolic effects of the androgens and somatic growth in man, Ann Int. Med 20:632-654, 1944.
44. Kenyon, A T, Knowlton, K., Sandiford, I, Koch F C., and Lotwin, G.: A comparative study of the metabolic effects of testosterone propionate in normal men and women and in eunuchoidism, Endocrinology 26:26-45, 1940.
45. Kepler, E. J., Sprague, R. G., Mason, H. L., and Power, M. H.: Aspects of clinical endocrinology: the pathologic physiology of adrenal cortical tumors and Cushing's syndrome, Rec. Progr. Hormone Res 2:345-389, 1948.
46. Kinsell, L. W.: ACTH and cortisone—after nearly four years of intensive clinical and experimental evaluation, J. Clin. Endocrinol. 13:120-122, 1955.
47. Kinsell, L. W., Boling, L., Partridge, J. W., and Foreman, N.: Corticotropin (ACTH) and cortisone; newer concepts of their use in clinical practice, California Med. 78: 487-490, 1953.
48. Kinsell, L. W., Hertz, S., and Reifenstein, E. C., Jr.: The effect of testosterone compounds upon the nitrogen balance and creatine excretion in patients with thyrotoxicosis, J. Clin. Invest. 23:880-890, 1944.
49. Kinsell, L. W., Margen, S., Michaels, G. D., McCallie, D. P., Anderson, C. T., Sutter, L. E., Thompson, V. T., Olson, F. E., and Signorotti, B. T.: Studies in fat metabolism: II. Evaluation of the effect of testosterone propionate upon ketone, carbohydrate, and protein metabolism in a patient with diabetes mellitus complicated by thyrotoxicosis, J. Clin. Invest. 30:1486-1490, 1951.
50. Knowlton, K., Kenyon, A. T., Sandiford, I., Lotwin, G., and Fricker, R.: Comparative study of metabolic effects of estradiol benzoate and testosterone propionate in man, J. Clin. Endocrinol. 2:671-684, 1942.
51. Kochakian, C. D.: The protein anabolic effects of steroid hormones *in* Harris, R. S., and Thimann, K. V. (eds.): Vitamins and Hormones, vol. 4, pp. 255-310, New York, Acad. Press, 1946.
52. Kountz, W. B., Ackermann, P. G., and Kheim, T.: The influence of some hormonal substances on the nitrogen balance and clinical state of elderly patients, J. Clin. Endocrinol. 13:534-547, 1953.
53. Landau, R. L., Knowlton, K., Lugibihl, K., Brandt, M., and Kenyon, A. T.: The anabolic effects of chorionic gonadotropin in normal young men, J. Clin. Invest. 29:619-629, 1950.
54. Luder, J.: Vertebral collapse after cortisone therapy, Great Ormond St. J. 7:15-21, 1954.

55. McCullagh, E. P., and Rossmiller, H. R.: Methyl testosterone: III. Effect upon body weight and growth, J. Clin. Endocrinol. 1: 507-510, 1941.

56. Parson, W., Crispell, K. R., and Ebbert, A., Jr.: Abnormalities in n-15 excretion rates after ingestion of tagged glycine in Cushing's syndrome and following ACTH administration, J. Clin. Invest. 31:548-554, 1952.

57. Paschkis, K. E., Herbut, P. A., Rakoff, A. E., and Cantarow, A. A case of Cushing's syndrome with adrenal cortical hyperplasia, without pituitary basophilic adenoma or hyperplasia, J. Clin Endocrinol. 3:212-217, 1943

58. Pearson, O. H., and Eliel, L P . Hormone therapy in cancer: experimental studies with ACTH and cortisone in patients with neoplastic disease, Rec. Progr Hormone Res. 6:373-416, 1951

59. Perloff, W H., Rose, E., and Sunderman, F. W.: Therapeutic observations in Cushing's syndrome. effect of various agents on calcium, phosphorus, and nitrogen excretion in a patient with pituitary basophilism, Arch. Int. Med. 72:494-505, 1943.

60. Rakoff, A. E , Cantarow, A., and Paschkis, K. E.: Cushing's syndrome (two cases treated with stilbestrol), J. Clin Endocrinol 1:912-915, 1941

61 Reifenstein, E. C., Jr.. Sect 3· Metabolic disorders of bone, Ch. 98: Osteoporosis *in* Harrison, T. R. (ed.): Principles of Internal Medicine, ed 2, pp 699-706, New York, Blakiston Division of McGraw-Hill, 1954.

62 ——— The protein anabolic activity of steroid compounds *in* Tr. Conf on Metabolic Aspects of Convalescence, Including Bone and Wound Healing, Supp No. 1, New York, Macy, 1942.

63. ———. The rationale for the use of anabolic steroids in controlling the adverse effects of corticoid hormones upon protein and osseous tissues, South. M. J. 49:933-960, 1956.

64. Reifenstein, E. C., Jr., and Albright, F.: The metabolic effects of steroid hormones in osteoporosis, J. Clin. Invest. 26:24-56, 1947.

65. Reifenstein, E. C., Jr , Albright, F., and Wells, S. L : The accumulation, interpretation, and presentation of data pertaining to metabolic balances, notably those of calcium, phosphorus, and nitrogen, J. Clin Endocrinol. 5:367-395, 1945; Correction, *ibid.*, 6:232, 1946.

66. Robinson, W. D., Boland, E. W., Bunim, J. J., Crain, D. C., Engleman, E. P., Graham, W., Lockie, L. M., Montgomery, M. M., Ragan, C., Ropes, M. W., Rosenberg, E. F., and Smythe, O. J.: Rheumatism and arthritis: review of American and English literature of recent years (tenth rheumatism review), Ann. Int. Med. 39: 498-618 and 757-906, 1953.

67. Sobel, H., and Marmorsten, J.: The effect of cortisone on the collagen and hexosamine content of the skin and femurs of one-year-old rats, Endocrinology 55:21-27, 1954.

68. Soffer, L. J , and Bader, R.: Corticotropin and cortisone in acute disseminated lupus erythematosus: results of long-term use, J A.M.A. 149:1002-1008, 1952.

69. Soffer, L. J , Elster, S. K., and Hamerman, D J.. Treatment of acute disseminated lupus erythematosus with corticotropin and cortisone, A M A Arch. Int. Med. 93:503-514, 1954.

70. Sprague, R. G., Mason, H. L , and Power, M H.: Chemistry, physiology, and clinical endocrinology of the adrenal cortex: physiologic effects of cortisone and ACTH in man, Rec Progr. Hormone Res. 6:315-372, 1951.

71. Sprague, R. G., Power, M. H., Mason, H. L., Albert, A., Mathieson, D. R., Hench, P S., Kendall, E. C., Slocumb, G. H., and Polley, H. F.: Observations on the physiologic effects of cortisone and ACTH in man, Arch. Int. Med. 85:199-258, 1950.

72. Steinbrocker, O., Ehrlich, M E., Silver, M., Sicher, W., Berkowitz, S., Carp, S., and Feinstein, H.: The clinical application of cortisone and ACTH in arthritis and related conditions. methods and problems. Part II: Side-effects, complications, contraindications, precautions, and conclusions Arizona Med. 6:29-35, 1951.

73 Talbot, N. B , and Butler, A. M.: Urinary 17-ketosteroid assays in clinical medicine, J. Clin Endocrinol. 2:724-729, 1942.

74. Talbot, N. B., Sobel, E. H., McArthur, J. W., and Crawford, J. D.: Functional Endocrinology, From Birth Through Adolescence, p. 330, Cambridge, Mass., Harvard, 1952.

75. ———.*Op cit* , p. 418.

76 Talbot, N B , Zygmuntowicz, A. S , Wood, M , and Christo, E.: Ch. 4: Observations

urine: a survey of the use of this test in endocrine investigation, diagnosis and therapy, J. Clin. Endocrinol. 1:234-256, 1941.

31. Gill, A. M.: Treatment of Cushing's syndrome with large doses of oestrin, Lancet 233:70-72, 1937.
32. Goldzieher, M. A.: Growth and sex hormones, J. Clin. Endocrinol. 1:924-927, 1941.
33. Gordan, G. S.: Evaluation and use of anabolic steroids, GP 10:87-102, 1954.
34. Greenlee, R. G.: Hyperfunction of the adrenal cortex, M. Clin. North America 39:1081-1099, 1955.
35. Hamburger, C.: Normal urinary excretion of neutral 17-ketosteroids with special reference to age and sex variations, Acta endocrinol. 1:19-37, 1948.
36. Hamilton, H. B., and Hamilton, J. B.: Ageing in apparently normal men: I. Urinary titers of ketosteroids and of alpha-hydroxy and beta-hydroxy ketosteroids, J. Clin. Endocrinol. 8:433-452, 1948.
37. Henneman, P. H., Irwin, J. W., Wang, D. M. K., and Burrage, W. S.: The effect of estrogen and androgen on calcium metabolism during cortisone administration, J. Clin. Endocrinol. 15:858, 1955.
38. Hubble, D.: Cushing's syndrome and thymic carcinoma, Quart. J. Med. 18:133-147, 1949.
39. Ingle, D. J.: Some studies on the role of the adrenal cortex in organic metabolism, Ann. New York Acad. Sc. 50:576-595, 1949.
40. Irwin, J. W., Henneman, P. H, Wang, D. M. K., and Burrage, W. S: Maintenance cortisone in intractable asthma: preliminary observations of undesirable cortisone effects, J. Allergy 25:201-209, 1954
41. Kenyon, A. T.: The effect of testosterone propionate on the genitalia, prostate, secondary sex characters, and body weight in eunuchoidism, Endocrinology 23:121-134, 1938.
42. Kenyon, A. T., Knowlton, K., Lotwin, G., Munson, P. L., Johnston, C. D., and Koch, F C: Comparison of the metabolic effects of testosterone propionate with those of chorionic gonadotropin, J. Clin. Endocrinol 2:685-689, 1942
43. Kenyon, A. T., Knowlton, K., and Sandiford, I: The anabolic effects of the androgens and somatic growth in man, Ann. Int. Med 20:632-654, 1944
44. Kenyon, A. T., Knowlton, K., Sandiford, I., Koch F. C, and Lotwin, G.: A comparative study of the metabolic effects of testosterone propionate in normal men and women and in eunuchoidism, Endocrinology 26:26-45, 1940.
45. Kepler, E. J., Sprague, R. G., Mason, H. L., and Power, M. H.: Aspects of clinical endocrinology: the pathologic physiology of adrenal cortical tumors and Cushing's syndrome, Rec. Progr. Hormone Res. 2:345-389, 1948.
46. Kinsell, L. W.: ACTH and cortisone—after nearly four years of intensive clinical and experimental evaluation, J. Clin. Endocrinol. 13:120-122, 1955.
47. Kinsell, L. W., Boling, L., Partridge, J. W., and Foreman, N.: Corticotropin (ACTH) and cortisone; newer concepts of their use in clinical practice, California Med. 78: 487-490, 1953.
48. Kinsell, L. W., Hertz, S., and Reifenstein, E. C., Jr.: The effect of testosterone compounds upon the nitrogen balance and creatine excretion in patients with thyrotoxicosis, J. Clin. Invest. 23:880-890, 1944.
49. Kinsell, L. W., Margen, S, Michaels, G. D, McCallie, D. P., Anderson, C. T., Suiter, L. E., Thompson, V. T., Olson, F. E., and Signorotti, B. T.: Studies in fat metabolism: II. Evaluation of the effect of testosterone propionate upon ketone, carbohydrate, and protein metabolism in a patient with diabetes mellitus complicated by thyrotoxicosis, J. Clin. Invest. 30:1486-1490, 1951.
50. Knowlton, K., Kenyon, A. T., Sandiford, I., Lotwin, G., and Fricker, R.: Comparative study of metabolic effects of estradiol benzoate and testosterone propionate in man, J. Clin. Endocrinol. 2:671-684, 1942.
51. Kochakian, C. D.: The protein anabolic effects of steroid hormones *in* Harris, R. S., and Thimann, K. V. (eds.): Vitamins and Hormones, vol. 4, pp. 255-310, New York, Acad. Press, 1946.
52. Kountz, W. B, Ackermann, P. G., and Kheim, T.: The influence of some hormonal substances on the nitrogen balance and clinical state of elderly patients, J. Clin. Endocrinol. 13:534-547, 1953.
53. Landau, R. L., Knowlton, K., Lugibihl, K, Brandt, M., and Kenyon, A T.: The anabolic effects of chorionic gonadotropin in normal young men, J. Clin. Invest. 29:619-629, 1950.
54. Luder, J.: Vertebral collapse after cortisone therapy, Great Ormond St. J 7:15-21, 1954.

55. McCullagh, E. P., and Rossmiller, H. R.: Methyl testosterone: III. Effect upon body weight and growth, J. Clin. Endocrinol. 1: 507-510, 1941.
56. Parson, W., Crispell, K. R., and Ebbert, A., Jr.: Abnormalities in n-15 excretion rates after ingestion of tagged glycine in Cushing's syndrome and following ACTH administration, J. Clin. Invest. 31:548-554, 1952.
57. Paschkis, K. E., Herbut, P. A., Rakoff, A. E., and Cantarow, A.: A case of Cushing's syndrome with adrenal cortical hyperplasia, without pituitary basophilic adenoma or hyperplasia, J. Clin. Endocrinol. 3:212-217, 1943.
58. Pearson, O. H., and Eliel, L. P.: Hormone therapy in cancer: experimental studies with ACTH and cortisone in patients with neoplastic disease, Rec. Progr. Hormone Res. 6:373-416, 1951.
59. Perloff, W. H., Rose, E., and Sunderman, F. W.: Therapeutic observations in Cushing's syndrome: effect of various agents on calcium, phosphorus, and nitrogen excretion in a patient with pituitary basophilism, Arch. Int. Med. 72:494-505, 1943.
60. Rakoff, A. E., Cantarow, A., and Paschkis, K. E.: Cushing's syndrome (two cases treated with stilbestrol), J. Clin. Endocrinol. 1:912-915, 1941.
61. Reifenstein, E. C., Jr.: Sect. 3: Metabolic disorders of bone, Ch. 98: Osteoporosis *in* Harrison, T. R. (ed.): Principles of Internal Medicine, ed. 2, pp. 699-706, New York, Blakiston Division of McGraw-Hill, 1954.
62. ———: The protein anabolic activity of steroid compounds *in* Tr. Conf. on Metabolic Aspects of Convalescence, Including Bone and Wound Healing, Supp. No. 1, New York, Macy, 1942.
63. ———: The rationale for the use of anabolic steroids in controlling the adverse effects of corticoid hormones upon protein and osseous tissues, South. M J. 49:933-960, 1956.
64. Reifenstein, E C., Jr, and Albright, F.: The metabolic effects of steroid hormones in osteoporosis, J. Clin. Invest. 26:24-56, 1947.
65. Reifenstein, E C., Jr., Albright, F., and Wells, S L.: The accumulation, interpretation, and presentation of data pertaining to metabolic balances, notably those of calcium, phosphorus, and nitrogen, J. Clin Endocrinol. 5:367-395, 1945; Correction, *ibid.*, 6:232, 1946.
66. Robinson, W. D., Boland, E. W., Bunim, J. J., Crain, D. C., Engleman, E. P., Graham, W., Lockie, L. M., Montgomery, M. M., Ragan, C., Ropes, M. W., Rosenberg, E. F., and Smythe, O. J.: Rheumatism and arthritis: review of American and English literature of recent years (tenth rheumatism review), Ann. Int. Med. 39: 498-618 and 757-906, 1953.
67. Sobel, H., and Marmorsten, J.: The effect of cortisone on the collagen and hexosamine content of the skin and femurs of one-year-old rats, Endocrinology 55:21-27, 1954.
68. Soffer, L. J., and Bader, R.: Corticotropin and cortisone in acute disseminated lupus erythematosus: results of long-term use, J.A.M.A. 149:1002-1008, 1952.
69. Soffer, L. J., Elster, S. K., and Hamerman, D. J.: Treatment of acute disseminated lupus erythematosus with corticotropin and cortisone, A.M.A. Arch. Int. Med. 93:503-514, 1954.
70. Sprague, R. G., Mason, H. L., and Power, M. H.: Chemistry, physiology, and clinical endocrinology of the adrenal cortex: physiologic effects of cortisone and ACTH in man, Rec. Progr. Hormone Res. 6:315-372, 1951.
71. Sprague, R. G., Power, M. H., Mason, H. L., Albert, A., Mathieson, D. R., Hench, P. S , Kendall, E. C., Slocumb, G. H., and Polley, H. F.: Observations on the physiologic effects of cortisone and ACTH in man, Arch. Int. Med. 85:199-258, 1950.
72. Steinbrocker, O., Ehrlich, M. E , Silver, M., Sicher, W., Berkowitz, S., Carp, S., and Feinstein, H.: The clinical application of cortisone and ACTH in arthritis and related conditions: methods and problems Part II: Side-effects, complications, contraindications, precautions, and conclusions. Arizona Med. 6:29-35, 1951.
73. Talbot, N. B., and Butler, A. M.: Urinary 17-ketosteroid assays in clinical medicine, J. Clin. Endocrinol. 2:724-729, 1942.
74. Talbot, N. B., Sobel, E. H , McArthur, J. W , and Crawford, J. D.: Functional Endocrinology, From Birth Through Adolescence, p. 330, Cambridge, Mass., Harvard, 1952.
75. ———:*Op. cit.*, p. 418.
76. Talbot, N. B., Zygmuntowicz, A. S., Wood, M , and Christo, E.: Ch. 4: Observations

on adrenal cortical "sugar-fat-nitrogen" hormone ("11-17-OCS") and "17-ketosteroid precursor" production by normal and abnormal individuals of various ages with comments on the fact that (a) there may be two ACTH's and (b) the normal adrenal cortex may not produce true androgens *in* Mote, J. R. (ed.): Proc. First Clin. ACTH Conf., pp. 32-37, New York, Blakiston Division of McGraw-Hill, 1950.

77. Teabeaut, R., Engel, F. L., and Taylor, H.: Hypokaliemic, hypochloremic alkalosis in Cushing's syndrome: observations on the effects of treatment with potassium chloride and testosterone, J. Clin. Endocrinol. 10:399-409, 1950.
78. Teicher, R., and Nelson, C. T.: Osteoporosis and pathological fractures following treatment with ACTH and cortisone, J. Invest. Dermat. 19:205-210, 1952.
79. Thompson, W. O., Thompson, P. K., and Taylor, S. G., 3rd: Production of sexual maturity in young women with primary amenorrhea, Tr. A. Am. Physicians 56:75-76, 1941.
80. Thorn, G. W., Jenkins, D., Laidlaw, J. C., Goetz, F. C., Dingman, J. F., Arons, W. L., Streeten, D. H. P., and McCracken, B H.: Pharmacologic aspects of adrenocortical steroids and ACTH in man, New England J. Med. 248:232-245, 284-294, 323-337, 369-378, 414-423, 588-601, 1953; (Concluded) Clinical uses of ACTH, cortisone, and hydrocortisone: specific replacement therapy, New England J. Med. 248:632-646, 1953.
81. Varangot, J.: Granulosa Tumors (Ovary Folliculomas), Paris, Arnette, 1937.
82. Welch, R. G., and Forsyth, C. O.: Still's disease treated with ACTH and cortisone, Great Ormond St. J. 5:1-6, 1953.
83. Wells, B B, and Kendall, E. C.: The influence of cortisone and c-17-hydroxydehydrocorticosterone (compound E) on somatic growth, Proc. Staff Meet., Mayo Clin. 15:324-328, 1940.
84. West, H. F., and Newns, C. R.: Cortisone and rheumatoid disease, Lancet 265: 1123-1126, 1953.
85. Whitelaw, M. J.: A case of Cushing's syndrome treated with testosterone propionate, J. Clin. Endocrinol. 4:480-482, 1944.
86. Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, p. 157, Springfield, Ill., Thomas, 1950.
87. Wilkins, L., and Fleischmann, W.: The influence of various androgenic steroids on nitrogen balance and growth, J. Clin. Endocrinol. 6:383-401, 1946.

Therapia a Steroides Anabolic in le Tractamento de Depletion Proteinic e de Osteoporosis Inducite per Hormones Corticoide

Summario in Interlingua

Therapia a steroides anabolic, in quantitates adequate e pro tempores sufficiente, es indicate pro *restaurar* le proteina e le histos ossee in patientes qui suffre de depletion proteinic e/o de osteoporosis associate con le syndrome de Cushing ab lesiones benigne, con etates avanciate, con le stato postmenopausal, con hypogonadismo e normal functiones adrenocortical, e con prolongate e/o intense therapia corticoide.

Therapia a steroides anabolic, in quantitates adequate e pro tempores sufficiente, es indicate pro *prevenir* effectos adverse super le proteina e le histos ossee (a) in patientes comenciante un regime de chronic medicationes corticoide e (b) in personas con manifestationes del avantiamento del etate, in feminas al menopause e post illo, e in patientes con hypogonadismo e normal functiones adrenocortical.

In patientes sub chronic therapia corticoide, le dosage de steroide anabolic deberea esser mantenite a un nivello sufficiente pro prevenir hypercalcuria (que es un indication de effectos adverse de hormon corticoide super le osso).

Un combination de androgeno con estrogeno es apparentemente le plus potente e le plus practic preparato anabolic nunc disponibile tanto pro le tractamento como etiam pro le prevention del effectos adverse de hormones corticoide super le proteina e le histos ossee.

8

Developmental Affections of the Skeleton Characterized by Osteosclerosis

C. L. HINKEL, M.D., MED. SC. D.*

There are a number of interesting developmental abnormalities of the skeleton which are characterized by an increase in bone density. Generally speaking these are uncommon, and differential diagnosis is a challenging problem. Some of these conditions, such as osteopetrosis and osteopoikilosis, are well known, but others which must be considered in differential diagnosis are to be found only in small numbers or in obscure sources.

It is the purpose here to review, discuss and illustrate insofar as possible the characteristics of each. Authors from this and other countries have been kind enough to furnish roentgenograms of illustrative cases, some of which have been published previously. These are reproduced here in the hope that they may be of comparative value in differential diagnosis.

Osteosclerosis is always a finding of radiologic diagnostic significance. In developmental conditions such familiar etiologic factors as tumor, trauma, infection and extrinsic toxic substances can be ruled out. In the abnormal osseous states discussed here the increased density must be attributed either to excessive bone deposition or to deficient resorption. One must consider the sclerosis to be a manifestation of disturbed physiology.

Theories of pathogenesis in developmental sclerotic bone conditions must be formulated on the insecure basis of scanty biopsy material and a few sporadic necropsies. A great deal is not understood, and some of the most widely accepted "fundamentals" are based upon supposition. In most of the sclerotic conditions it appears that the bone of increased density is qualitatively normal in composition but is increased in amount per unit volume. In young growing bones the sclerotic areas are usually the result of deficient physiologic osteoclasis. In adult bones (which are also undergoing simultaneous new bone formation and osteoclasis at a slower rate) the sclerosis often is the result of osteoblastic overactivity.

Generally it is accepted that hypervascularity of bone results in demineralization or halisteresis. On the other hand, osteosclerosis is probably related to hypovascularity and relative local anoxia. This concept is supported by animal experimentation.[6] It is well to recognize that numerous factors, such as abnormally resistant matrix, osteoblastic overactivity, upsets in local acid-base balance, the choking of haversian canals, congenital vascular defects, microscopic emboli and deficient capillary invasion, may be of great significance in pathogenesis.

Because most of these affections show a strong familial tendency,[14,18,30] and since abnormalities often can be recognized *in utero*, it is believed that the basic defect is in the

* Director, Department of Radiology, George F. Geisinger Memorial Hospital, The Foss Clinic, Danville, Pa.

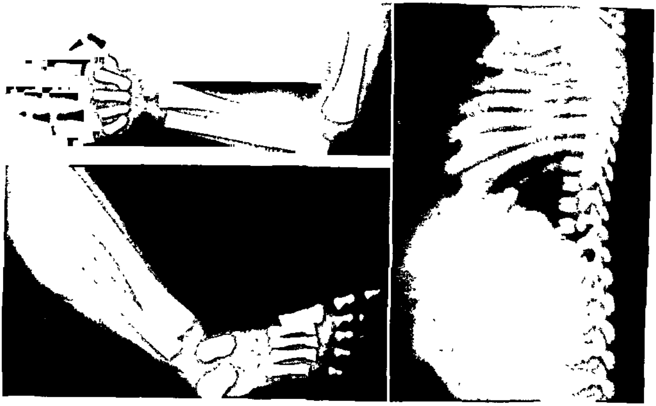


FIG. 1. Osteopetrosis (malignant) in a 6-month-old child. All the bones are involved, and the spleen is enlarged. (Dr. John Caffey)

primordial mesenchyme, which is the forerunner of all osteogenic tissues. This is particularly well documented in the pathologic studies of osteopetrosis.[5,27,34]

The classic diagnostic characteristics of diseases of the skeleton such as we are discussing are not always encountered in pure form. It is not surprising that there are borderline cases which do not fit perfectly into any one clear category. Perhaps some of these constitute "missing links" between other classic entities Possibly, for instance, osteopathia striata is a transition stage between osteopetrosis and osteopoikilosis. Perhaps Ribbing's disease is a mild late form of Engelmann's disease. All we can say is that at present there are a number of sclerotic osseous diseases which appear to be sufficiently different to justify separate designation and description.

Roentgenologic Approach. In the roentgenologic evaluation of polyostotic or *systemic osteosclerosis it is necessary to have* survey roentgenograms of the entire [illegible] ton. Opinions based upon incomplete study are frequently incorrect. Patients should be seen in person, and in all cases a family history must be included, since skeletal abnormality in a sibling or a relative may make the diagnosis clear

Although a number of the skeletal abnormalities to be discussed are discoverable clinically, fortuitously others are recognized by the radiologist in the course of some other examination. In most cases the roentgenologic characteristics furnish the most valuable differential diagnostic information. *Since the skeleton lends itself admirably to* roentgenologic study, and anatomic variations can be shown pictorially, we shall lay emphasis upon the radiologic aspects and distributional patterns of each condition.

OSTEOPETROSIS

Osteopetrosis (marble bones; Albers-Schönberg's [illegible]; osteosclerosis fragilis [illegible] [illegible]elopmental disease of the [illegible] is characterized by



FIG. 2. Osteopetrosis (benign) in the hands and the foot of a 60-year-old male. There is perfect symmetry in the hands. The "bone within a bone" is well seen in the os calcis. (Hinkel & Beiler: Am. J. Roentgenol. 74:50 & 61)

marked increase in density of practically all bones. There are two fairly distinct clinical varieties of this disease. These are usually designated as (1) malignant and (2) benign. There is a strong familial tendency.

Malignant Form (Acute Fulminating; Severe Infantile Form)

This unquestionably begins *in utero* and is fatal at or soon after birth. Undoubtedly, numerous stillborn and fetal infantile cases go unrecognized The disease has been diagnosed *in utero*. The patients have large heads, poor dentition, dental caries and eye disturbances. The last mentioned may be in the forms of exophthalmus, nystagmus or severe optic atrophy. Skull involvement usually produces stenosis of vital foramina. There are severe anemia and enlargement of the spleen and the liver with extramedullary hematopoiesis Such infants usually survive only a few years, but they are underdeveloped or dwarfed, anemic, subject to infections (particularly osteomyelitis) and mentally retarded. The fragility of their bones may give rise to considerable deformity from fractures.

Although the severity of bone involvement is closely related to the length of survival of the infant, there is not always a direct relationship between the severity of the anemia and the extent of medullary obliteration.

Radiologically the appearance is unmistakable. Practically all the bones of the skeleton are increased in density, the medullary spaces are narrowed, and there is little or no trabecular pattern. The metaphyses of the long bones are clubbed or flask shaped. Fine striations in the cortices and transverse and longitudinal lines of relatively increased density are found in the metaphyses. All the long bones, the pelvis, the spine and the ribs are symmetrically and markedly involved. In the skull the sclerosis is typically marked in the base. Figure 1 illustrates this form.

Benign Adult Form

In this form of the disease the diagnosis is almost always made roentgenologically, since the anemia, the splenic enlargement, the dwarfing and the neurologic changes so characteristic of the infantile malignant form usually are absent. The mere fact of survival is in itself evidence of the essentially benign nature of the generalized disease. Chemical and blood studies are negative.

Radiologically there is a tendency for most of the long and flat bones of the skeleton to be involved, but some bones may be spared. The disease shows certain characteristic distribution patterns and roentgenologic appearances. The pelvis, the spine, the ribs and the diaphyses of the long bones are almost invariably involved in such a charac-

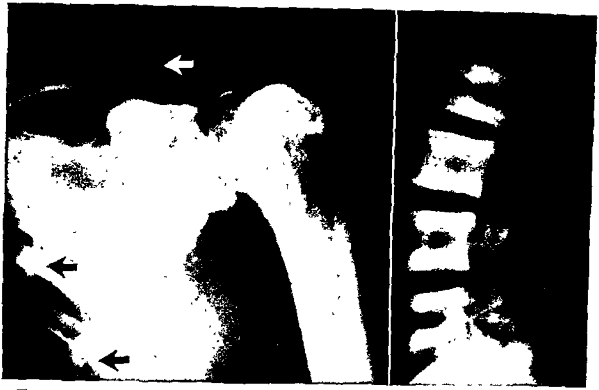


FIG. 3. Osteopetrosis in male adult, brother of patient shown in Figure 2. Osteopetrotic central area in humeral head *(left)* probably represents unresorbed juvenile bone. Arrows indicate sclerotic nidi in ribs and clavicle. "Sandwich" vetebrae are well exemplified at right. (Hinkel & Beiler: Am. J. Roentgenol. 74:56 & 59)

teristic manner that the roentgenologic diagnosis can be made unequivocally. Involvement of distal portions of the skeleton, such as hands, wrists, feet and distal tibias, is much less constant. Involvement of the

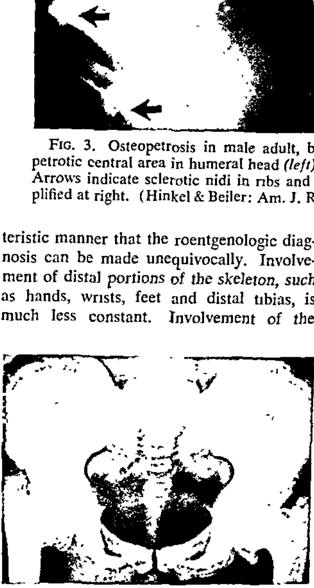


FIG. 4 Osteopetrotic pelvis. Symptomatic male, aged 60. Broad iliac bands stand out clearly Bilateral coxa vara results from unrecognized femoral neck fractures. (Hinkel & Beiler. Am. J. Roentgenol. 74:51)

facial bones and the skull appears to be largely a familial characteristic. In the family reported by Higinbotham and Alexander, for instance,[13] all members of the family showed prognathism and sclerotic mandibles. Other families have shown leontiasis osseum. In general, however, the bones of the face usually are spared, as they were in our own series. In all cases of osteopetrosis the involvement is strikingly symmetric, a finding which is shown well in the hands of a 60-year-old male in Figure 2 *(left)*.

We have previously reported 5 siblings with adult osteopetrosis[14] which was not recognized until between the ages of 55 and 64. The familial distribution pattern and the symmetric sclerosis were very characteristic. Some of the typical roentgenologic findings are illustrated in Figures 2 to 5. The "bone within a bone" appearance, "sandwich" vertebrae, metaphyseal sclerosis, bowing and clubbing, and the ringlike laminated structure of the iliac bones are all characteristics of specific differential diagnostic value.



FIG. 5. Mild adult osteopetrosis in 58-year-old brother of patient shown in Figure 4. Although the distribution is the same, the changes are much less marked. The "bone within a bone" appearance is well exemplified. (Hinkel & Beiler: Am.. J. Roentgenol. 74:49, 51 & 55)

Discussion of Adult Osteopetrosis

It has been well established that patients with this disease are subject to remissions and exacerbations which unquestionably explain the alternating lines of increased and decreased density found in the regions of the iliac crests and in the metaphyses. The persistence of the dense osteocartilaginous inclusion and dense transverse or vertical lines is attributed to deficient bone resorption which is believed by most to be the inherent bone defect responsible for the ivorylike density. Many patients with the skeletal involvement of this kind give a history of multiple fractures which may or may not heal well. Most of the reported patients have led relatively normal lives. One of our patients (not illustrated) who had even more marked and more diffuse bone involvement than any of his siblings was completely symptom free at the age of 64. He enjoyed an active and a successful business career, raised a family and was playing golf daily at the time the radiologic diagnosis was established. One of his brothers (aged 60), however—a mechanic—had symptoms of pain and limitation of motion in both hips. He was found to have marked sclerosis of the pelvis, unrecognized old bilateral fractures of the femoral necks "sandwich" vertebrae, sclerotic long bones, extensive involvement of the ribs and other typical manifestations of osteopetrosis, some of which are illustrated in Figure 3. His pelvis and hips are shown in Figure 4. One of his siblings, showing much less marked involvement, presented the appearance illustrated in Figure 5.

As is almost universally the case, all chemical studies, hematologic studies and clinical findings were within normal limits. Frequently, upon study of roentgenograms, one can find evidence that new normal bone was laid down on top of pre-existing osteopetrotic bone. This manifestation usually is seen best in the carpal bones, tarsal bones, vertebrae and ilii. Bone of markedly different densities can be identified in the os calcis shown in Figure 2. After extensive study, including bone biopsy, there appeared to be adequate justification for the assumption that the disease of osteopetrosis began in this patient at about 3 years of age and continued in an intermittent fashion until near puberty.

PATHOLOGY OF OSTEOPETROSIS

In both types of osteopetrosis the bones are grossly heavy, thick, dense, hard and brittle. When the bone is fractured it cracks



FIG. 6. Photomicrograph. Femoral head of patient in Figure 4. Magnification × 100. Nests of unresorbed cartilage cells lie in dense bone of abnormal pattern. These cartilage cells should have been resorbed in adolescence. Osteopetrosis in 60-year-old male. (Hinkel & Beiler: Am. J. Roentgenol. 74:57)

and splinters much as glass does (a characteristic of considerable orthopaedic importance). The medullary cavity is reduced in size or absent. Histologically there is an excess of dense bone and matrix, which for some reason is not resorbed in the normal physiologic manner. Probably the bone is abnormally resistant to the forces of resorption. Zawisch-Ossenitz[34] believes that as a result of a defect in the bone-forming blastema, the bone and the matrix resist physiologic resorption. Dense cement lines, excess osteoid tissue, islands of cartilage cells and scanty marrow elements characterize the histologic appearance. This is illustrated in Figure 6, which shows a photomicrograph of the femoral head of one of our patients. There is always a relative increase in lamellar bone, and defects in the haversian systems usually are present. Sectioned bones studied under polarized light reveal a scarcity of fibrils which is believed to be related to the unusual fragility. Osteoclasts are recognizable, but, since islands of unresorbed bone, densely calcified matrix and recognizable cartilage cells are found even in aged individuals, it is evident that physiologic resorption is grossly deficient.

Differential Diagnosis

Generally the radiologic differential diagnosis in cases of osteopetrosis is not a serious problem, since typically the characteristics are unmistakable. In atypical cases, however, differentiation from other generalized osteosclerotic processes of various etiologies must be accomplished. Some of the conditions which must be considered are listed here. This is an unusually long list, since many conditions characterized by diffuse osseus sclerosis must be considered.

Myelosclerosis (Osteosclerotic Anemia). The osteosclerosis is generalized but usually less severe than in osteopetrosis. Since the disease is essentially one of fibrosis and replacement of the medullary cavities, there are always progressive severe anemia and splenomegaly. Transverse lines of density near the metaphyses are absent; there is no familial tendency; the disease appears in adult life and is associated with a downhill clinical course.

Fluorosis (Fluoride Poisoning). Individuals working in fluoride mines or exposed to cryolite may develop diffuse sclerosis of the skeleton.[11,27] This is different from osteopetrosis in that not all growth centers are involved, there is extensive calcification of ligamentous and paravertebral structures, the skull is not affected and there is no clubbing, striation or bowing of the long bones. There is no radiologic involvement of the skull. The teeth may be discolored and mottled. Chemical and histologic studies of the bone are diagnostic, and of course the history of fluoride exposure is of great value.

Lymphoblastomas. Occasionally in Hodgkins' disease or leukemia the skeleton becomes increased in density. Here the involvement is rarely symmetric, there usually are splenomegaly, lymphadenopathy and anemia. The characteristic "sandwich vertebra," "bone within a bone" appearance and basilar skull involvement of osteopetrosis are absent. The downhill course and the clinical manifestations are valuable in differentiation.

Metastatic osteoblastic carcinoma (of the prostate or breast), when extremely disseminated, may manifest itself in practically every bone in the body, resulting in generalized and possibly symmetric osteosclerosis. However, there is absence of parallel and transverse striations, clubbing, "bone within a bone" appearance and involvement of ossification centers. The clinical diagnosis frequently is obvious, and there is elevation of the acid and/or alkaline phosphatase.

Paget's Disease. Although this gives rise notably to generalized increase in density of the bones, the involvement is rarely truly symmetric, and the coarsening of the trabeculae, enlargement of the vertebrae, the bowing of the long bones, the onset late in life and chemical studies make differential diagnosis relatively easy.

Heavy Metal Poisoning. Heavy metals, such as lead, bismuth and phosphorus, may give rise to metaphyseal sclerosis, but this occurs only during the growth period and is not found in adult life. There is relative sparing of the skull and the small bones of the hands and the feet. The possibility of heavy metal poisoning during the growth period must always be considered in the adult benign form of the disease, but study of the entire skeleton and a careful history permit the exclusion of such toxic substances.

Osteopathia Striatum (Voorhoeve's Disease). This condition, which probably is related in some way to osteopetrosis, will be discussed later in this chapter. While there is a superficial local resemblance to osteopetrosis, the metaphyseal localization and the heterogeneous striped densities cannot be confused easily. On the *other hand, in* osteopetrosis there may be a marked local resemblance to osteopathia striatum, as is illustrated in Figure 5 *(right).*

Engelmann-Camurati's Disease (Progressive Diaphyseal Dysplasia). While this disease may involve multiple long bones, and usually is sclerotic, the diaphyseal sclerosis with relative sparing of the metaphyses and the absence of clubbing should permit ready differentiation from osteopetrosis. The importance of radiologic study of the entire skeleton cannot be overemphasized.

Infantile Cortical Hyperostosis (Caffey's Disease). In infants this condition, which is characterized by the deposition of subperiosteal new bone, may simulate marble bones. The characteristic involvement of the mandible, the clavicles and the shoulder girdles, the clinical manifestations of soft-tissue swelling, fever and spontaneous recovery permit ready differentiation.[2]

Melorheostosis, osteopoikilosis and hyperostosis corticalis generalisata, which conceivably may be considered in the radiologic differential diagnosis, will be discussed below. In all instances, general skeletal survey roentgenograms should permit of accurate differentiation.

OSTEOPATHIA STRIATA (VOORHOEVE'S DISEASE)

This abnormality is characterized by striation in the metaphyses of long bones.

Radiologic

On radiologic examination the outstanding feature of this condition is striation of any or all of the bones with the exception of the skull and the clavicles. There is relative sparing of the hands. The striation is parallel to the long axis of the bones, and it involves the metaphyses principally. At times it may extend into the adjacent epiphysis. When the ilia are involved, the lines radiate toward the iliac crests, producing a striking fanlike arrangement and resembling the cartilaginous columns seen in dyschondroplasia. Small bony exostoses frequently are found in large-bone metaphyses and in the pelvis. The condition usually is bilaterally symmetric. Frequently the striations can be seen well in the os calcis. Sometimes islands of dense bone are found interspersed among the streaks. The dense striations are very similar to the smaller dense osseous islands



FIG. 7. Osteopathia striata in the lower extremities of a 3-year-old female. The striations were found also in other metaphyseal regions. (Bloor, D. U.: J. Bone & Joint Surg. 36B:263)

in osteopoikilosis. The lower extremity striations are shown well in Figure 7.

Clinical

Usually there are no symptoms of this condition. It has been reported in children below the age of puberty and also in adults of all ages. It is believed to be caused by congenital developmental defect, possibly related to dyschondroplasia or osteopoikilosis. Vague recurrent joint pains have been reported, but in most patients the bone abnormality is asymptomatic. It is more common in males than in females. There is a very definite familial tendency. In Voorhoeve's original report[33] the condition was found in a father and his two children.

Pathology

So far as we can determine, nothing is known about the pathology or the histology of this condition.

Differential Diagnosis

Dyschondroplasia, which may simulate or duplicate the striations of this disease, is usually more prominent in the distal long bones, while in osteopathia striata the bones of the hands and the feet are seldom affected.

Osteopoikilosis. In some cases of osteopoikilosis the small oval dense islands of bone may be elongated, simulating the streaks in osteopathia striata. Probably these two diseases are related, and it is possible that they represent somewhat different manifestations of the same process, as has been suggested by Lindbom.[21] Usually, however, osteopoikilosis involves the epiphyses and small bones of the extremities more than osteopathia striata.

Osteopetrosis. This disease may sometimes produce vertical and parallel striations in the metaphyses which are very similar to those found in osteopathia striata. The similarity usually is most marked in the proximal tibias, as seen in Figure 5 *(right)* Osteopetrosis can be differentiated only by study of the entire skeleton.

OSTEOPOIKILOSIS (OSTEOPATHIA CONDENSANS DISSEMINATA; OSTEOPECILIA; OSTEITIS CONDENSANS DISSEMINATA; SPOTTED BONES; BENIGN BONE ISLANDS)

This abnormality of the skeleton is char-



Fig. 8. Osteopoikilosis. Asymptomatic male, aged 43. The dense islands were found in practically all epiphyseal and metaphyseal regions.

acterized by the presence of multiple dense islands in cancellous bones.

Radiologic

Radiologic manifestations consist of small dense ovoid circular or fusiform islands of dense bone ranging from about 2 to 10 mm. in greatest dimension. These are particularly numerous and typical in the epiphyses and the metaphyses adjacent to epiphyseal lines. They are also numerous in the carpals and the tarsals. The appearance is illustrated in Figure 8. The islands are found only in cancellous bone. When they are numerous, as they frequently are about the acetabula, they may be superimposed or conglomerate, giving rise to irregularly geographic-shaped islands of compact bone 2 cm. or more in diameter. The dense islands are rare in the diaphyses of long bones but tend to be clustered in the metaphyses and the epiphyses They have been observed to change in size[16] The skull is seldom involved. The cortex is uninvolved, and there is no change in external contour or in the soft tissues

Clinical

No symptoms are attributed to the abnormality of the bones. There are no spontaneous fractures Skin lesions (dermatofibrosis lenticularis disseminata) are *sometimes* associated.[21] All chemical and blood studies are normal. The condition is much more common in males than in females, and usually the radiologic diagnosis is established in early adult life. There is a very definite hereditary tendency, and the abnormality may occur in succeeding generations.[15,27]

Pathology

On cross section of bones the dense islands are readily identifiable. Microscopically the appearance is that of condensed cancellous bone. The individual islands consist of regularly arranged trabeculae, and there is no connection with the epiphyseal cartilage or associated fibrotic change in the medullary cavity. The cortical bone is normal in appearance.

Differential Diagnosis

Usually the radiologic appearance is so characteristic that differentiation is not difficult.

Multiple small osteoblastic metastatic lesions usually can be ruled out without difficulty. Skeletal survey roentgenograms are very desirable.

Dyschondroplasia, which is sometimes characterized by spotty dense islands near the epiphyseal lines and in the pelvis, can be excluded on the basis of the normal appearance of the epiphyseal lines and the absence of the stippling of the secondary ossification centers which is typical of osteopoikilosis.



FIG. 9. Melorheostosis in 34-year-old female. The flowing hyperostoses are visible in the pelvis, femur, tibia and lateral bones of the foot, where there is deformity of contour. These are recent films of patient reported in 1943 by Carpender *et al*, Am. J. Roentgenol. 49:398)

MELORHEOSTOSIS (LERI TYPE OF OSTEOPETROSIS; FLOWING HYPEROSTOSIS)

This is a very rare bone condition characterized by osteosclerosis involving parts of some bones. The sclerosis follows a peculiar "flowing" distribution pattern. It tends to be unilateral.

RADIOLOGIC

Radiologically the condition is characterized by the presence of dense structureless and marblelike areas in parts of long bones. There is a strong tendency for the petrosis to extend throughout the length of the limb, but there is seldom complete petrosis of the encircling cortex The term *flowing* is used in an effort to describe the resemblance to melted wax flowing down the side of a burning candle. When the upper extremity is involved it is common to see the peculiar subcortical and cortical petrotic bone involving the scapula, the humerus and one or both of the bones of the forearm, as well as the fingers. In the lower extremity the abnormality frequently is seen in one side of the pelvis and throughout the lower extremity, extending into the metatarsals and the phalanges. Figure 9 illustrates some of the recent roentgenograms of a 34-year-old woman in whom the diagnosis was established at the age of 9. This patient had an unusual bilateral distribution pattern, which has been reported previously.[4]

In advanced cases there are cortical distortion and enlargement of involved bones. When the dense patches of bone involve the carpal and the tarsal regions, it appears to be largely endosteal. Frequently the uneven splotches of petrotic bone simulate spilled or

splashed paint. In relatively early cases the joints are spared, even though the long bones proximal and distal to the joint are involved. If the disease progresses, the joints become involved. Deposits of abnormal dense bone in the soft tissues are sometimes found in the knee, shoulder, hip and ankle.

The ribs, spine and skull almost always escape involvement, but a few isolated cases have been reported in which even these portions of the skeleton were affected.[10]

Clinical

This condition has been observed in both sexes, but males are affected more commonly than females. There is no known hereditary or familial tendency. Cases have been reported from 5 to 50 years of age. It is generally believed to begin in childhood, but probably in some cases the onset is *in utero*.

This condition is symptomatic. Most patients complain of some pain, which is dull and aching in character and seldom severe, and may be exaggerated by exertion. Limitation of movement of one or more of the joints involved by the disease is quite frequent. The deposition of bone in soft tissues and involvement of the periarticular structures probably are related to the symptoms. Local swelling, induration and erythema may occur. Frequently, when the cortex is irregularly thickened, this can be palpated, particularly in the phalanges. Deformity of the bone, which can be detected clinically, results from asymmetric thickening coupled with limitation of movement, but other congenital abnormalities such as genu valgum, curvature of the spine and flatfoot frequently have been associated.[10] Scleroderma also has been reported to complicate this condition.[7]

Course

This disease usually is slowly progressive. Some patients have been observed for many years and the petrosis has shown gradual increase. There are exceptions, however, since other young patients have been observed for a period of years and the lesions have shown neither progression nor regression.

Pathology

Grossly the dense bone is indistinguishable from osteopetrosis. Histologic findings indicate that the dense areas are the result of localized osseous sclerosis. There is overcrowding of lamellae, these being arranged in a bizarre manner. There is an interlacing pattern of bone trabeculae, and there is dense concentric perivascular ossification. The number of osteoblasts is increased, and the haversian canals are thick walled.

All laboratory and blood chemical tests are within normal limits.

Differential Diagnosis

The bizarre appearance of the streaky longitudinally arranged osteopetrotic bone is generally so characteristic that differential diagnosis is not difficult.

The disease should be differentiated without difficulty from osteopetrosis and from osteopoikilosis by study of the entire skeleton. The possibility of chronic pyogenic osteomyelitis may well be considered on the basis of the sclerotic deformed and irregular appearance of the small bones of the hands and the feet, but in general the limitation of the abnormality to one side of tubular bones permits of differentiation.

ENGELMANN'S DISEASE

Engelmann's disease (Camurati-Engelmann's disease; osteopathia hyperostotica multiplex infantalis; progressive diaphyseal dysplasia) is a very uncommon bone condition characterized by symmetric fusiform enlargement and sclerosis of the shafts of the long bones. Usually it is encountered between 3 and 10 years of age. It is associated with neuromuscular signs and symptoms.[20,23,29]

Radiologic

The radiologic characteristics are typical.

There are fusiform enlargement and sclerosis of the middle thirds of the shafts of long bones, most commonly the femurs and the tibias. The radius, the ulna and the fibula also may be involved. The anatomic changes are symmetric, even though the symptoms are unilateral. The clavicles and the humeri seldom are involved, and, although the sclerotic changes have been described in the pelvic bones, the scapula, the mandible and the metacarpals—in most cases hands, feet, ribs and spine—escape involvement. The external surfaces of the involved diaphyses present a smooth but dense appearance. At first glance the appearance suggests local cortical thickening, but there is no separate subperiosteal layer (onion peel) of dense cortex. The medullary cavity is reduced in width. The lower extremities of involved children are unusually long and slender.

Neuhauser *et al.*,[24] who were the first to report this disease in this country, showed gradual progression of the lesions along the long axis of the bone in both proximal and distal directions. Two of Neuhauser's patients showed sclerosis of the base of the skull and involvement of the hands, feet, pelvis and spine in addition to the major long bones. The changes in the femurs over an interval of 5 years are very well shown in Figure 10.

Clinical

These patients are underweight and show muscular atrophy, tenderness on deep pressure, waddling gait, muscular fatigue and occasional inequality in the length of extremities. Frequently they have abnormal reflexes and neurologic changes of a nonspecific character.

All laboratory examinations are within normal limits. There is no leukocytosis.

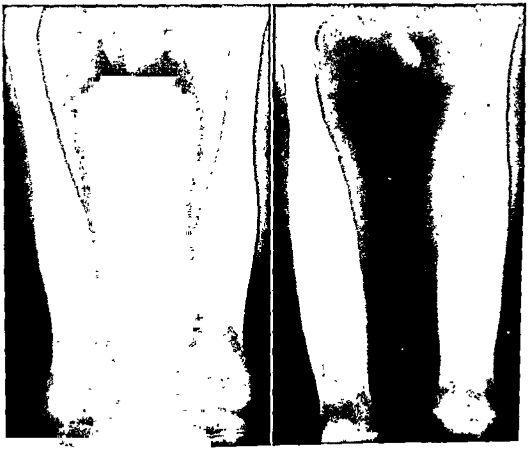


Fig. 10 Engelmann's disease Femurs of a boy at 4 years of age *(left)* and at 9 years of age *(right)* illustrate the progressive nature of the diaphyseal dysplasia. (Neuhauser, E. B , *et al.*: Radiology 51:18)

There is no evidence of hereditary or familial tendency. Males are involved somewhat more commonly than females. Prognosis is good, although, as mentioned before, there generally is slow progression and extension of the osteosclerotic process.

Pathology

Grossly the appearance of the bones suggests progressive subperiosteal new bone apposition with a decrease in the thickness of the compact layer. Histologically it is found that the cortical bone is being altered to cancellous bone while the periosteum is actively laying down new bone. The marrow cavity presents the appearance of rapid reconstruction of bone, and there is local replacement of the marrow fat by fibrosis. The disturbance in bone architecture is different from any pattern that might result from normal growth mechanisms. The new cortical bone shows lack of normal trabecular pattern and presents an amorphous appearance. There is no mosaic pattern such as is found in Paget's disease. There is no histologic evidence to suggest an inflammatory agent. It is assumed that the disease is related to certain extraskeletal organs because of the neurologic and the muscular changes, failure to gain weight and other associated manifestations.

Differential Diagnosis

Chronic Sclerosing Osteomyelitis. If only one bone or one limb is studied, this diagnosis must be strongly suspected. It should be ruled out on the basis of fever, leukocytosis, rapid progression and radiologic study of other portions of the skeleton, which will disclose the disease to be symmetric and multicentric in Engelmann's disease.

Infantile Cortical Hyperostosis (Caffey's Disease) in young children may closely simulate the radiologic appearance. This, however, occurs in the first year of life, is accompanied by fever, and there is spontaneous recovery within a few months. Typically, this condition involves the mandibles and the shoulder girdles.



Fig. 11. Ribbing's disease. Diaphyseal dysplasia of hereditary type in a 20-year-old male without neurologic or muscular abnormalities. (Paul, L. W.: Radiology 60:414)

Osteopetrosis. This disease should be excluded readily, since it tends to affect the metaphyses and to spare the diaphyses.

HEREDITARY MULTIPLE DIAPHYSEAL SCLEROSIS (RIBBING'S DISEASE)

This abnormality, which is very much like Engelmann's disease in many respects, was first reported in 1949 by Ribbing[26] and has been described in this country by Paul.[25] The condition consists of diaphyseal sclerosis and enlargement in the long bones of two or more members of the same family. It is believed to represent a familial dysplasia without known cause. Although the radiologic appearance of diaphyseal widening and dense sclerosis is very similar to that of Engelmann's disease, there are certain points of difference in the nonradiologic characteristics. The disease occurs at or after puberty and is not associated with neurologic changes, muscular dystrophy, abnormal gait, fatigue or any other manifestations except local bone pain. Ribbing's cases ranged from 17 to 32 years of age, while Paul's patients were aged 20 and 35. The roentgenograms in Figure 11 show a striking resemblance to those of Engelmann's disease.

Differential Diagnosis

The differential diagnosis in this condition is the same as in Engelmann's disease. There are no important qualitative or quantitative roentgenologic differential criteria. The condition is distinguished from Engelmann's disease by its later onset, familial occurrence and absence of neuromuscular abnormalities.

HYPEROSTOSIS GENERALISATA WITH PACHYDERMIA (UEHLINGER'S DISEASE; ACROMEGALOID OSTEOSIS; IDIOPATHIC FAMILIAL GENERALIZED OSTEOPHYTOSIS; CHRONIC IDIOPATHIC HYPERTROPHIC OSTEOARTHROPATHY)

This is a generalized familial skeletal dissease beginning between 13 and 18 years of age and progressing into adult life. The changes involve the skin and the subcutaneous tissues and the skeleton.

Radiologic

Radiologically there is marked increase in the breadth of the long and the short tubular bones of the extremities without overgrowth in length. The long bones resemble columns or pillars. The diaphyses are broader than the epiphyses because of subperiosteal new bone growth. Early in the disease there may be slightly serrated or spicular margins of the long bones, but later, when these serrations are filled in by bony bridges, the compact layer is greatly thickened and its differentiation from the medullary cavity is difficult. There are coarse bone trabeculation and some mottling in the denser areas. Osteophytes may be numerous in the pelvis and the scapulae. The ribs and the clavicles show cortical thickening, and the vertebrae present a coarsely trabeculated sclerotic appearance somewhat suggestive of Paget's disease. Usually the skull, the facial bones and the mandible are spared. There is also sparing of the small bones of the hands and the feet. Late in the disease there may be fusion of the carpal and the tarsal bones and ossification of the ligaments of the spine and of the interosseous membranes in the forearm and the leg. Figure 12 from Uehlinger illustrates the unusual characteristics of this conditions.

Clinical

Clinically the lower extremities (hands and forearms) of the patient have an elephantiasislike appearance, and there is pachydermia of the forehead and the scalp. The skin of the forehead and the scalp lies in thick folds, and there is usually pronounced sweating. The fingers are clubbed, and the joints are painful and stiffened. Patients complain of rheumaticlike joint pains, easy fatigability and limitation of motion in joints which may progress to ankylosis. Thickening of the skin of the face and the eyelids may produce a sleepy expression.



FIG. 12. Hyperostosis generalisata with pachydermia. The long bones resemble massive columns. The pelvis suggests Paget's disease. (Cocchi, U., *in* Schinz, H. R., *et al.*: Roentgen Diagnostics, ed. 5, Stuttgart, Thieme)

Pressure on spinal nerve roots may result from local osteophytic spurring and may cause neuromuscular disturbances and loss of sphincteric control.

The disease is distinctly familial, and it is much more common in males than in females All laboratory and chemical tests are normal.

Pathology

Bone biopsy indicates marked periosteal overgrowth and a peculiar palisade arrangement of osseous ridges and trabeculae in the bones of the trunk and the extremities. Normal trabecular structure is replaced by a coarse meshwork of crisscross trabeculae which tend to follow the lines of stress. The newly formed bone shows mature lamellar structure. The marrow spaces are filled with fat but are not fibrotic. It appears that the new bone which is deposited subperiosteally is in the form of spongiosa. The skeleton actually is increased in size. The skull, when it is involved, shows only endosteal hyperostosis.

Differential Diagnosis

Hypertrophic osteoarthropathy (chronic pulmonary osteoarthropathy of Bamberger-Marie)[3] must of course be considered. This is essentially the same disease process in a milder form, but it is secondary to pulmonary disease, and it is encountered frequently in elderly individuals.

Paget's Disease. Although, when certain bones such as the vertebrae and the pelvis are involved, they may resemble those of Paget's disease, the latter can be excluded on the basis of age, facial appearance, absence of soft-tissue involvement and normal blood chemical studies.

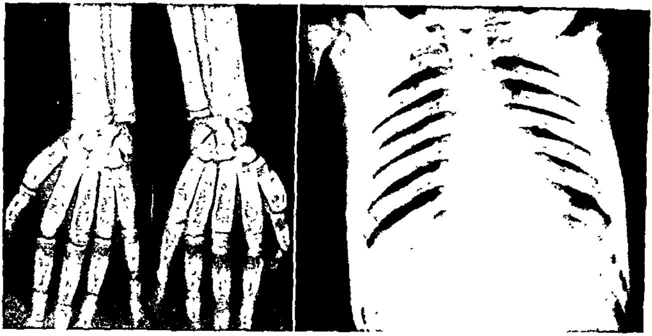


FIG. 13. Halliday's hyperostosis. Female, aged 7. In addition to the changes in hands, clavicles and ribs, there was marked skull and facial involvement. (Halliday, John: Brit. J. Surg. 37:54 & 55)

VARIANTS OF HYPEROSTOSIS CORTICALIS GENERALISATA

Generalized cortical hyperostosis has been described in various forms which are believed to deserve separate mention and description. Three of the atypical or variant forms are reviewed briefly here

HYPEROSTOSIS GENERALISATA WITH STRIATIONS (FAIRBANK'S DISEASE)

Fairbank[11] has reported the case of a 28-year-old male who had generalized osteosclerosis, *coarsened bone texture, cortical* thickening and hyperostosis of long bones, pelvis and spine, and in addition osseous striations in the metaphyses and the calcanei similar to those of osteopathia striata. The peculiar admixture of hyperostosis and striation was present in the pelvis and also in the hands and the feet.

The nature of the disease is not known, and its exact place in the schema of bone diseases has not been determined as yet.

HALLIDAY'S DISEASE

Halliday, of Australia,[12] described a case of unusual bone dystrophy in a girl who was studied from 3 to 10 years of age. The bones of the face were greatly thickened, the mouth could not be closed, there was advanced *optic atrophy and nerve deafness,* and the child showed retarded mentality. The head was large.

Radiologically the skeleton was found to *be markedly sclerotic in some areas, particularly* in the skull, maxillary regions, ribs and clavicles. The changes in the skull very much resembled Paget's disease. The ribs were extremely thick, dense and club shaped. The clavicles were about three times normal size and were markedly increased in density. The bones of the lower extremities showed thinning of the sticklike shafts of the cortex and widening of the medullary spaces. The arms and the hands showed normal epiphyseal development and sausagelike metacarpals and phalanges with thinned cortices. The changes in the hands were practically identical with those of *Engelmann's disease. Figure 13 shows some* of Halliday's roentgenograms.

The child died, and necropsy studies of the bones were carried out. Histologically the bones of the skull, the clavicles and the



FIG. 14. Generalized familial hyperostoses with neurologic changes. Hands, ribs and feet of 48-year-old male. Twin of this patient was similarly involved. (Van Buchem, F. S. P., *et al.*: Acta radiol. 44:110 & 112)

ribs were found to be extremely dense and sclerotic. Numerous osteoblasts were present. The haversian canals varied in size, and the medullary cavities were unusually fibrotic. No diploic spaces were present in the skull. The transition between the compact and the spongy portions of the bone was abrupt. A continuous layer of osteoblasts bounded the compact portion. Bony trabeculae were covered with osteoblasts. The vertebrae were essentially normal except for evidence of overactivity of osteoblasts.

It appears from study of the roentgenograms, the distribution pattern and the histopathologic changes that this disease is different from Engelmann's disease, osteopetrosis and melorheostosis. Of course, it is possible that the changes might be attributed to the osteitic type of leontiasis osseum with associated rib- and long-bone involvement.

Generalized Hyperostosis with Neurologic Changes (Van Buchem's Disease)

Van Buchem[32] described two cases of familial hyperostosis corticalis generalisata which, while showing considerable similarity to Uehlinger's disease and also to Engelmann's disease, appear to be sufficiently dissimilar to justify separate description. The two patients were twins in whom osteosclerotic diffuse skeletal changes with marked skull involvement was discovered at 48 years of age in the male and at 52 in the female. Both patients had exophthalmus, low mentality, visual disturbances, cranial nerve involvement and papilloedema.

Radiologic

The skull, the facial bones and the mandible showed very marked osteosclerosis and enlargement. There were marked thickening and sclerosis of the cortex of long bones and also of the short bones of the extremities, involving particularly the diaphyses with relative sparing of the epiphyseal ends. The diameter of the tubular bones was increased, especially in the diaphyseal portion, and this was associated with extensive osteophyte formation. The metacarpals, the metatarsals and the phalanges, as well as the ribs, were involved extensively, but there was relative sparing of the pelvis and the spine. The generalized involvement of the skull, mandible, ribs and clavicles appears to be practically indistinguishable from osteopetrosis. The diaphyseal involvement of the long bones appears radiologically to be essentially the same as in Engelmann's disease. The roentgenologic appearance is shown in Figure 14. The general texture of the osteosclerosis, the relative sparing of the ends of

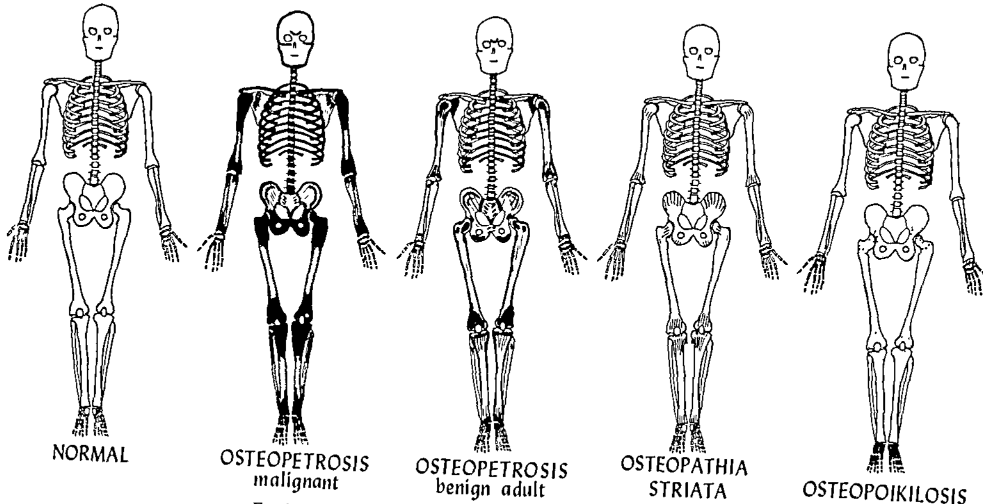


FIG. 15. Diagrammatic representation of skeletal differential characteristics and distribution patterns in conditions discussed.

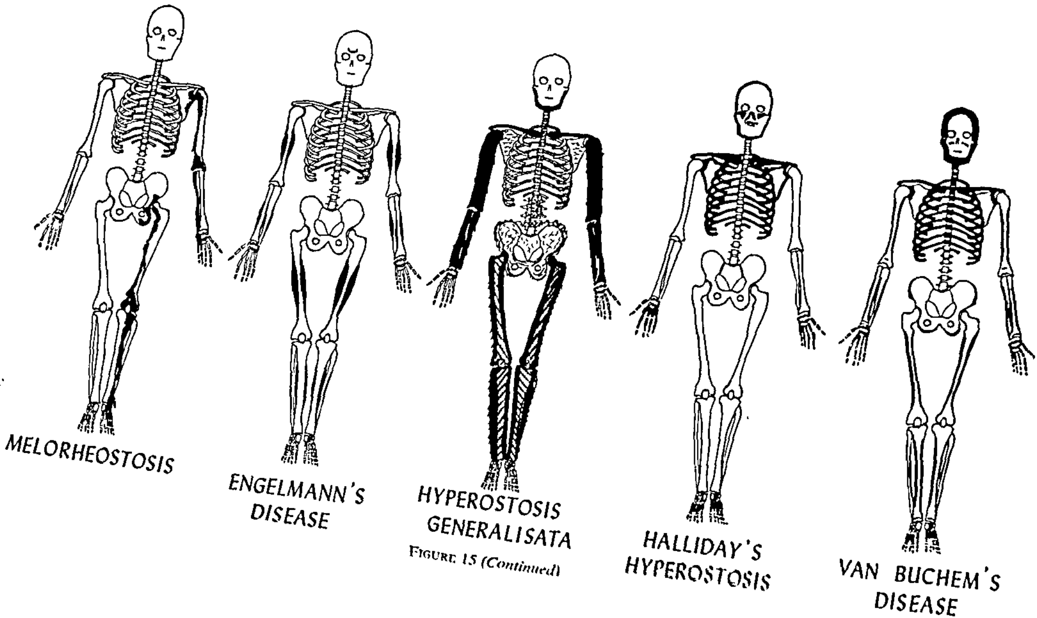


FIGURE 15 (Continued)

long bones and the absence of pachydermia of the head and the extremities are the principal diagnostic features differentiating this condition from Uehlinger's disease (hyperostosis generalisata with pachydermia).

Clinical

Clinically patients with this rare abnormality are mentally deficient, tire easily and have exophthalmus, together with loss of vision and hearing. The face is misshapen, due largely to osseous enlargement and sclerosis of the facial bones and particularly the mandible. There is no pachydermia or bone pain. In the female there is loss of secondary sex characteristics indicative of hypopituitarism. There is considerable limitation of motion of the spine, which may be rigid. Laboratory tests and blood studies are noncontributory.

Pathology

The involved bone is greatly thickened, extremely sclerotic and heavy. The surfaces of involved bones showed small ragged excrescences and osteophytes. The cortex of the long and the short bones is greatly thickened and sclerotic, but there is sparing of the epiphyseal ends. Chemical composition of the bone is within normal limits. Osteoblasts and osteoclasts are present in normal numbers, and there is no evidence of recent bone destruction. The medullary cavities are decreased in size, but otherwise the bone marrow is normal without sclerosis The pituitary gland is small

Differential Diagnosis

Osteopetrosis. In osteopetrosis the changes are extremely similar in qualitative appearance, but the distributional pattern is different Involvement of the vertebrae, the pelvis and the metaphyses are absent in Van Buchem's disease.

Osteomyelosclerosis. In this disease the blood picture is abnormal, there is extramedullary hematopoiesis, and the course is downhill Usually the osteosclerosis involves spine and pelvis and spares the small bones and the skull.

Hyperostosis Generalisata with Pachydermia (Uehlinger's Disease). This condition begins in puberty with pain and swelling of the joints. Pachydermia is present in the scalp, the arms and the legs, and usually there is clubbing of the fingers. The skeleton is increased in size, and the bone texture as seen radiographically is somewhat similar to that of Paget's disease.

Engelmann's Disease. The symmetric osteosclerosis of the diaphyses of long bones and phalanges is very similar in these two conditions. In Engelmann's disease the skull is spared and spine involvement is slight. The abnormal gait, muscle wasting, relatively long extremities and early age of onset (found in the latter condition) also serve as differential points.

SUMMARY

A number of osteosclerotic developmental abnormalities of the skeleton have been presented. In most instances the clinical and roentgenologic characteristics are sufficiently specific to permit of accurate diagnosis. Since the distribution patterns usually are important in differential diagnosis, these are illustrated diagrammatically in Figure 15. No drawing is included to represent Ribbing's disease, since this is indistinguishable from Engelmann's disease.

REFERENCES

1. Bloor, D U.: A case of osteopathia striata, J. Bone & Joint Surg. 36B:261, 1954.
2. Caffey, J., and Silverman, W. A : Infantile cortical hyperostosis, Am. J. Roentgenol. 54:1, 1945.
3. Camp, J. D., and Scanlan, R L.: Chronic idopathic hypertrophic osteoarthropathy, Radiology 50:581, 1948.
4. Carpender, J W. J., Baker, D. R., Perry, S. P., and Outland, T.: Melorheostosis, Am. J. Roentgenol. 49:398, 1943.
5. Cohen, J.: Osteopetrosis; case report, autopsy findings and pathological interpretation, J. Bone & Joint Surg. 33A:923, 1951.
6. Coolbaugh, C. C · Effects of reduced

blood supply to bone, Am. J. Physiol. 169: 26, 1952.
7. Dillehunt, Richard B., and Chiunard, Eldon G.: Melorheostosis leri, J. Bone & Joint Surg. 18:991, 1936.
8. Engelmann, G.: Ein Fall von Osteopathia hyperostitica (scleroticans) multiplex infantilis, Fortschr. Röntgenstr. 39:1101, 1929.
9. Evans, John: Leontiasis ossea; a critical review with reports of four original cases, J. Bone & Joint Surg. 35B:229, 1953.
10. Fairbank, H. A. T.: Melorheostosis, J. Bone & Joint Surg. 30B:533, 1948.
11. Fairbank, Thomas: An Atlas of General Affections of the Skeleton, London, Livingstone, 1951.
12. Halliday, J.: A rare case of bone dystrophy, Brit. J. Surg. 37:52, 1949.
13. Higinbotham, N. L., and Alexander, S. F.: Osteopetrosis; four cases in one family, Am. J. Surg 53:444, 1941.
14. Hinkel, C. L., and Beiler, D D.: Osteopetrosis in adults, Am. J. Roentgenol. 74: 46, 1955.
15. Hinson, A.: Familial osteopoikilosis, Am. J. Surg. 45:566, 1939.
16. Holly, L. E.: Osteopoikilosis; a five year study, Am. J. Roentgenol. 36:512, 1936.
17. Hurt, R. L.: Osteopathia striata—Voorhoeve's disease, J. Bone & Joint Surg. 35B: 89, 1953.
18. Kelley, C. H , and Lawlah, J. W.: Albers-Schönberg disease—family survey, Radiology 47:507, 1946.
19. Kraft, Ernest: The pathology of monomelic flowing hyperostosis or melorheostosis, Radiology 20:47, 1933.
20. Lavine, L. S., and Koven, M T.: Engelmann's disease, J Pediat. 40:235, 1952.
21 Lindbom, A.· Zwei neue Fälle mit "streifenformiger Osteopoikilie" (Voorhoeve) Acta radiol. 23:296, 1942.
22. McPeak, C. N.: Osteopetrosis; report of eight cases occurring in three generations of one family, Am. J. Roentgenol. 36:816, 1936.
23. Michaelis, L. S.: Engelmann's disease, Proc. Roy. Soc. Med. 42:271, 1949.
24. Neuhauser, E. B., Schwachman, H., Wittenborg, M., and Cohen, J.: Progressive diaphyseal displasia, Radiology 51:11, 1948.
25. Paul, Lester W.: Hereditary multiple diaphyseal sclerosis (Ribbing), Radiology 60: 412, 1953.
26. Ribbing, S.: Hereditary multiple diaphyseal sclerosis, Acta radiol. 31:522, 1949.
27. Schinz, H. R., Baensch, W. E., Friedl, E., and Uehlinger, E.: Roentgen-Diagnostics, James T. Case (ed.), New York, Grune, 1951.
28. Sear, H. R.: Melorheostosis and the creeping periostotic form of leontiasis, Brit. J. Radiol. 20:470, 1947.
29. Singleton, Edward B., Thomas, John R., Worthington, W. W., and Hild, John R.: Progressive diaphyseal dysplasia (Engelmann's disease), Radiology 67:233, 1956.
30. Stein, Irvin, Stein, Raymond, and Beller, Martin: Living Bone in Health and Disease, Philadelphia, Lippincott, 1955.
31. Uehlinger, E.: Hyperostosis generalisata mit Pachydermie, Fortschr. Röntgenstr. 67:8, 1943.
32. Van Buchem, F. S. P., Hadders, H. N., and Ubbens, R.: An uncommon familial systemic disease of the skeleton: Hyperostosis corticalis generalisata familiaris, Acta radiol. 44:109, 1955.
33. Voorhoeve, N.: L'image radiologique non encore décrite d'une anomalie du squelette, Acta radiol. 3:407, 1924.
34. Zawisch-Ossenitz, C.: Marble bone disease; study of osteogenesis, Arch. Path. 43:55, 1947.

Affectiones Disveloppamental del Skeleto, Characterisate per Osteosclerose

Summario in Interlingua

Es passate in revista e illustrate un serie de anormalitates skeletic que es apparentemente de natura disveloppamental. Omne iste anormalitates es relativemente incommun, e le illustrationes ha essite colligite in numerose fontes in omne partes del mundo. Le physiologia pathologic del ossos sclerotic in iste gruppo de conditiones anormal non es ben comprendite. Il es probabile que in le majoritate del casos un factor fundamental

consiste in hypovascularitate local le qual, de su parte, resultarea de inherente defectos mesenchymal.

Le symptomas e le constatationes clinic es rarmente de character sufficientemente typic pro supportar le diagnose, e tests laboratorial es essentialmente sin valor. Del altere latere, le characteristicas roentgenologic forma configurationes definite, e le alterationes qualitative insimul con le modos de distribution es usualmente de character sufficientemente clar pro permitter le diagnose differential. Le plus utile criterios del diagnose differential es presentate discursivemente e in roentgenogrammas e diagrammas skeletic.

9

Multiple Myeloma

I. SNAPPER, M.D.*

ETIOLOGY

Multiple myeloma is a fatal disorder of the reticuloendothelial system characterized by the proliferation of young, abnormal plasma cells, by extensive destruction of the skeletal system and by marked disturbances in protein metabolism.

The nature and the pathogenesis of multiple myeloma remain obscure. Because the myelomatous infiltration of the bone marrow is associated occasionally with the presence of large numbers of plasma cells in the peripheral blood, many authors are of the opinion that myeloma represents the aleukemic form of plasma-cell leukemia. In this connection it should be stressed that myeloma differs in certain fundamental aspects from the true leukemic syndromes. The three unique disturbances in the protein metabolism, which are present in myeloma patients, do not occur in leukemia or in any other disease. This holds true for the Bence Jones proteinuria, for the characteristic myeloma globulins found at electrophoretic examination, and also for primary amyloidosis, which occurs in about 10 per cent of the myeloma patients.[10] For completeness it must be added that rarely has primary amyloidosis or paramyloidosis been observed in patients, where careful search failed to reveal signs of a myelomatous disease.

BENCE JONES PROTEINURIA

True Bence Jones protein is characterized by its behavior at different temperatures; it precipitates between 45° and 60° C., and dissolves again between 90° and 95° C.

When addition of sulfosalicylic acid solution to urine does not cause a precipitate, then no Bence Jones protein is excreted. When the precipitate, caused by addition of sulfosalicylic acid solution, dissolves on boiling, then the presence of Bence Jones protein is probable, and the more precise test of Jacobson and Wilner[25] should be performed. For the determination of Bence Jones protein only fresh urine should be used. If the protein content of the urine of a myeloma patient is 4+ or even higher, then the patient's urine should be diluted with normal fresh urine until the total protein of the mixture has been decreased to 2+. Ten cc. of fresh and adequately diluted myeloma urine is brought to a pH of 5.5 by the addition of a few drops of 2 per cent acetic acid. The pH is checked with nitrazine paper. Then the urine is heated in a water bath to approximately 60° C. and held at this temperature for 10 minutes. The urine is centrifuged and decanted. The sediment, containing the Bence Jones protein, is suspended in 10 cc. of normal urine. One drop of concentrated nitric acid is added for every cubic centimeter of urine, and the specimen is brought to a boil. If Bence Jones protein is present, the solution will clear on heating to 95° C. On cooling, the precipitate will reappear.

For many years it has been known that, apart from true Bence Jones protein, other abnormal protein derivatives frequently are encountered in the urine of myeloma pa-

---

* Brooklyn, N. Y.

tients. Some of these remarkable proteins precipitated at 45° C. but did not dissolve at 95° C., so-called pseudo-Bence Jones protein. Other substances, which did not precipitate at 45° C. to 60° C., but only at 70° to 75° C., did dissolve at 95° C., so-called proteoses. It is now recognized that part of the pseudo-Bence Jones proteins and proteoses, although no true Bence Jones protein, produce at electrophoretic examination such sharp and tall peaks that they decidedly belong to the myeloma proteins.[19] This additional knowledge has not diminished the diagnostic significance of true Bence Jones protein. In the presence of this substance *the diagnosis of myeloma is certain.*

SERUM PROTEINS

So long as only chemical methods were used for the determination of the serum globulin, hyperglobulinemia was found in about 60 per cent of the patients with multiple myeloma. Much more revealing are the results of the electrophoretic examination of myeloma sera. With this method, in order of decreasing frequency, characteristic tall elevations of the gamma, beta or alpha globulin peaks are found. Frequently an abnormal fraction (M protein) migrating between the beta and the gamma globulins is present. In this way the presence of abnormal globulins can be elicited in about 80 per cent of the myeloma sera. If both serum and urine of myeloma patients are examined electrophoretically the diagnostic importance of this method becomes still more evident. When only chemical methods are used for the determination of Bence Jones protein and serum globulins, about 12 per cent of the myeloma patients exhibit neither Bence Jones proteinuria nor hyperglobulinemia. In contrast, electrophoretic methods almost invariably demonstrate characteristic changes of serum and/or urinary proteins in myeloma.[20]

PARAMYLOIDOSIS

The localization of paramyloid, often designated as primary amyloid, differs completely from the customary findings in secondary amyloid. The latter develops after long-standing suppuration, arthritis, syphilis, leprosy and other diseases. Secondary amyloid is found mainly in liver, spleen, kidneys and adrenals. Sites of predilection for the deposition of paramyloid in myeloma are the joint capsules producing the clinical manifestations of rheumatoid arthritis, the myocardium resulting in congestive failure, the skin manifesting as bizarre, waxy, subcutaneous masses and alopecia, the gastrointestinal tract presenting as acute hemorrhages, the tongue causing macroglossia, and the larynx with ensuing difficulties in speech and deglutition. In addition, paramyloid may be present in other organs, as, for instance, lymph nodes and bone marrow. In all these organs paramyloid may be found in the form of hyaline masses. However, the main localization of paramyloid is in the walls of the blood vessels.[21] When paramyloidosis develops, Bence Jones proteinuria is nearly always present. At the same time the globulin content of the serum often is remarkably low.

PATHOLOGY

In multiple myeloma the bone involvement varies from diffuse proliferation of numerous myeloma cells to the formation of large tumorlike plasmocytomas. These plasmocytomas often erode through the cortex of the bone and may ultimately present as soft-tissue tumors.[5,23]

In most cases of multiple myeloma, both generalized myelomatosis and multiple plasmocytomas are present. Pathologic examination reveals widespread resorption of cancellous bone, destruction of cortical and cancellous bone by gray or hemorrhagic tumorlike plasmocytomas, associated with multiple fractures and deformities. Gross destruction of bone may be absent if the proliferation in the medullary cavity remains diffuse. In these cases the pathologic findings are limited to a generalized thinning of the cortex and destruction of the secondary bone trabecules. Microscopic examination

of the plasmocytomas reveals a strikingly monotonous picture of closely packed plasmoblasts with scanty stroma.

Extramedullary myelomatosis is present in spleen, liver and lymph nodes. Involvement of these organs too may consist of diffuse infiltration with myeloma cells and/or discrete nodules of cellular aggregates. Less frequently other organs show evidence of infiltration. Myelomatous infiltration of a testicle, simulating the presence of a primary testis tumor, has been observed.[16]

Uremia, a frequent cause of death in multiple myeloma, occurs only when Bence Jones protein is eliminated in the urine. In such cases a so-called myeloma kidney—enlarged, smooth and pale—results. The renal lesion, although not entirely specific, is characterized by extensive plugging of the tubules by large, dense eosinophilic casts. The casts, which frequently show calcified and lamellated centers, often extend into the proximal convoluted tubules.[18] Internal hydronephrosis due to the plugging of the tubules plays an important role in the pathogenesis of the renal insufficiency in myeloma. Although the glomeruli often appear to be intact at microscopic examination, renal clearance studies have demonstrated that in myeloma kidneys usually an associated disturbance in glomerular filtration exists.

THE MYELOMA CELL

Prior to the advent of the routine use of bone-marrow aspiration, studies of microscopic sections of bone marrow obtained at autopsy or at biopsy had led to the conclusion that multiple myeloma could be caused by rapid proliferation of any of the hematopoietic constituents of the bone marrow (plasma cells, myelocytes, myeloblasts, lymphocytes, etc.). Even multiple myeloma due to rapidly growing erythroblastomas has been described. This concept has vanished completely since bone-marrow aspiration by puncture has become popular. Bayrd,[1] employing this technic, concluded that the myeloma cell invariably was of the plasma-cell type. This conclusion has generally been confirmed.[3,25]

The appearance of the myeloma cell varies from a small, deeply basophilic, almost characteristic plasma cell to an immature, large, anaplastic plasmoblastic cell from 20 to 40 mc. in diameter. The nucleus of the myeloma cell is placed eccentrically, frequently contains one or two nucleoli and lacks the spoked-wheel arrangement of the chromatin network that characterizes the tissue-plasma cell. On the contrary, often the nucleus presents a closely knit reticulated appearance, with the chromatin arranged in sausagelike clumps. In the younger forms the nucleus usually is vesicular, with evenly distributed chromatin arranged in a fine network. Perinuclear halo formation is common, and myeloma cells containing several nuclei are encountered frequently. The large-cell type has either a pale or a dark-blue cytoplasm, sometimes containing vacuoles or, rarely, other inclusions. Myeloma cells, packed with pale-staining vacuoles, are referred to as Mott cells.[3] Some myeloma cells are studded with vacuoles containing a deep-staining substance. Occasionally the latter kind of vacuoles extend beyond the outer limits of the cytoplasm. Then a remarkable cell results which is designated by Stich *et al.* as a "grape cell."[26] In their experience the presence of this cell is pathognomonic of multiple myeloma. Large protein crystals can be found in myeloma cells and, incidentally, also in the renal tubular cells of patients with Bence Jones proteinuria.

INCIDENCE AND SURVIVAL

Myeloma usually is a disease of later life. While, rarely, its onset has been observed in young adults, the majority of cases occur between the ages of 40 and 70. There is no social or racial predilection. The wide global distribution is well illustrated by the increasing number of cases reported from Japan, where at least 76 cases have been observed.[13] This in all probability does not

represent a real increase in incidence, but is due mainly to local advances in diagnosis which permits of earlier recognition of the disease.

Myeloma invariably is fatal, the average duration of life being less than 1½ to 2 years after onset of symptoms. Occasionally patients survive for eight or more years, with or without treatment. Recently Bayrd has reported four such cases.[2]

The occurrence of multiple myeloma in different members of the same family must be a great rarity. One instance of a sister and a brother, both suffering from myeloma, has been reported.[17] Familial incidence of primary amyloidosis also occurs.[4]

CLINICAL FRACTURES

Bone Pain

Pain in the bones is the outstanding symptom of multiple myeloma and is present in about 90 per cent of the cases. The onset may be insidious with vague aches and pains, or it may be explosive—precipitated by a sudden pathologic fracture. As is the usual situation in destructive bone diseases, ultimately the pains become excruciating in character. The pains, which nearly always start in the lower back and ribs, are exacerbated by muscular effort. Even in the early stages of the disease, pain on pressure of the rib cage and limitation of the mobility of the spine can be elicited. Much less frequently does the pain start in other bony structures, as hips, legs, shoulders, arms, etc. In the later stages of the disease the pains may be located in almost any part of the skeleton. Severe lancinating pains may also be caused by involvement of nerve roots by vertebral collapse In the course of the disease the patient gradually becomes totally incapacitated, crying out with pain at the slightest bodily motion Occasionally there may be spontaneous pain-free remissions, but this is an unusual occurrence.

Pathologic fractures of one or more bones, predominantly in spine and ribs, occur in about 60 per cent of the patients. The long bones, sternum, clavicles and pelvis may be affected similarly. Pathologic fractures of the sternum are almost pathognomonic of multiple myeloma—at least in areas where osteomalacia does not occur. Fractures in multiple myeloma patients heal rapidly with remarkably good callus formation. Severe kyphoscoliosis with malformation of the thorax and shortening of the spine and the ribs approaching the rim of the pelvis occur commonly in the terminal stages.

Tumor Formation

Soft-tissue tumors may present themselves whenever a plasmocytoma has eroded through an underlying bone. Subcutaneous tumors occur most often, but not exclusively, over flat bones (e.g., sternum, ribs, pelvis, mandible, calvarium) and may reach the size of a melon. These subcutaneous plasmocytomas always are soft in consistency.

True nodular plasma-cell infiltrations of the skin do occur but are relatively uncommon manifestations [5,25]

Nervous System Involvement

Proliferation of plasmocytomas frequently leads to collapse of vertebral bodies. When the plasmocytic proliferation penetrates into the epidural space, lancinating pains due to compression of nerve roots, sometimes even transverse lesions of the cord, result. Among the noninflammatory diseases of the spine producing compression of the cord, only metastatic carcinoma occurs more frequently than plasmocytoma. The cranial cavity can be invaded with ensuing paralysis of cranial nerves or other cerebral signs. In addition, extensive and disabling neuritic pains may arise from an associated peripheral perineuritis.[9]

Renal Involvement

The marked renal insufficiency, which occurs in at least 20 per cent of the patients with multiple myeloma, is characterized by the absence of hypertension and retinitis In



FIG. 1. Pelvis and femora in multiple myeloma. All the bones present innumerable small punched-out osteolytic lesions without any sclerosis. There is a fracture of the left ischial bone, which is partially healed. As an incidental finding there is marked sclerosis of the iliac and the femoral arteries.

addition, outspoken edema is a rarity. The combination of azotemia, proteinuria and hyposthenuria in the absence of hypertension and edema may serve as the key to the diagnosis. This combination is rare except in myeloma and amyloid. Hematuria is also rarely, if ever, present The finding of Bence Jones proteinuria proves the presence of a myeloma kidney and excluded renal amyloidosis. On the other hand, extensive edema favors the diagnosis of secondary amyloid. Paramyloid of the kidneys, as observed frequently in multiple myeloma, is hardly ever extensive. Uremia in myeloma, associated with paramyloidosis, therefore, is not due to the amyloid but always to the deleterious action of Bence Jones protein upon the function of the kidneys.

Lymph Nodes, Liver and Spleen

Enlargement of the liver, often considerable, occurs in 40 per cent of the cases. Splenomegaly, which usually is less striking, is present in about one fourth of the patients. Generalized slight lymph-node enlargement by myelomatous infiltration of lymph nodes is found frequently. In most instances enlargement of liver and spleen is due to myelomatous infiltration, hardly ever to replacement by paramyloid. Lymph-node enlargement, however, may actually be due to paramyloid infiltration.

Treatment with urethane may also cause hepatosplenomegaly.[23,25]

OTHER FINDINGS

The absence of antibodies in the abnormal gamma globulin fraction of the myeloma serum is of considerable significance.[14,15] In the absence of antibodies in the serum a tendency to infections exists. Low-grade fever is present in about 40 per cent of the cases of multiple myeloma, and the initial stage of multiple myeloma may present as a "fever of unknown origin." In myeloma, inflammatory processes in the lungs are especially frequent, but meningitis too is a rather common complication. Recurring pneumonitis in adults is always a reason to suspect the possible presence of multiple myeloma.

In rare instances infiltration of small blood vessels with paramyloid results in bizarre

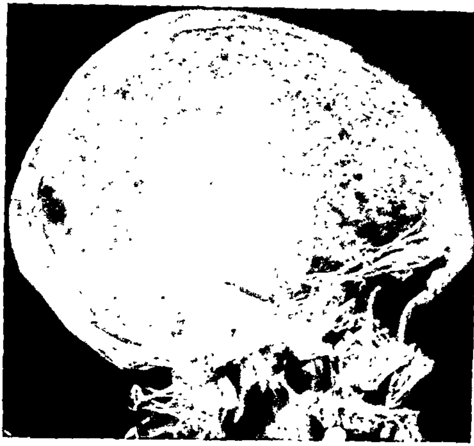


FIG. 2. Skull with multiple osteolytic lesions, perhaps somewhat less sharply delineated than usually seen in multiple myeloma.

pulmonary infiltrations.[28] Paramyloid may lead to many different clinical manifestations. Gastro-intestinal hemorrhages, widespread purpura and macroglossia already have been mentioned. In some unexplained cases of heart failure the autopsy has elicited the presence of paramyloid of the myocardium; *only at this late stage did* examination of the bone marrow reveal generalized myelomatosis. In one published case primary amyloid of the heart led to the clinical picture of constrictive pericarditis.[11]

ROENTGEN FINDINGS

Roentgen examination reveals that the most frequent sites of myelomatous infiltration are in the ribs, clavicles, sternum and spine; the skull, pelvis and proximal extremities (Fig. 1) also are involved frequently. However, any part of the skeleton may be affected, and even plasmocytomas of the phalanges have been described.[22,25]

The roentgenographic appearance may vary from diffuse, generalized "demineralization" to the presence of extensive melon-sized tumors with almost total bone destruction. The intramedullary expansion of multiple adjacent plasmocytomas may present a striking "soap-bubble" effect, such as seen in giant-cell tumors. When such a lesion is seen in one of the pelvic bones, the diagnosis of a plasmocytoma must always be considered. *The individual osteolytic lesions characteristically* are present as sharply demarcated punched-out holes which do not show any evidence of surrounding bony condensation.

The sievelike appearance of the calvarium in myeloma, due to an accumulation of innumerable plasmocytomas, is well known (Figs. 2 & 3). It should be realized that comparable roentgen pictures may be found occasionally in multiple metastases of a malignancy, especially of mammary cancer, or in a proliferating lymphoblastoma.[25] The differential diagnosis between these different affections may offer considerable difficulties. The following experience is sometimes helpful. Lymphoblastoma of the calvarium rather often breaks out of the skull and forms subcutaneous tumors, which always

FIG. 3. Skull with large sharply delineated punched-out osteolytic lesions, as seen in multiple myeloma.



are firm. In contrast, multiple myeloma of the skull only rarely leads to subcutaneous tumors, and such subcutaneous myelomas usually are soft.[25]

In vertebral collapse, due to multiple myeloma, as in malignancies, the intervertebral disk usually remains intact,[24] even if the adjacent vertebral bodies are completely collapsed (Fig. 4). In addition, paravertebral soft-tissue densities such as those seen in tuberculous spondylitis hardly ever are observed. However, exceptions do occur, and in rare instances myelomas leading to



FIG 4 [illegible] lytic lesior [illegible] tion of boı [illegible] higher than normal, indicating that the resistance of the vertebral bone has suffered considerably. In the upper part of the roentgenogram a compressed vertebra with intact adjacent disks is seen

destruction of the intervertebral disk with or without a paravertebral mass have been registered.[12] Notwithstanding the importance of the roentgen findings for the diagnosis of multiple myeloma, in about 5 per cent of the cases of this disease no demonstrable roentgen lesions of the skeleton can be elicited.[9,25,27] In such cases a generalized myelomatosis without macroscopic plasmocytoma is present. Until the bone resorption by the generalized myelomatosis has caused the disappearance of 30 to 40 per cent of the bone salts, the roentgenologic signs will be negligible.

LABORATORY FINDINGS

Peripheral Blood

Anemia is present in far the greater number of patients with multiple myeloma, and critically low hemoglobin values may develop. Leukocytosis is present in 20 per cent of the patients, and in one half of these cases a shift to the left is noted. Eosinophilia is seen occasionally. While the presence of a small number of plasma cells is noted in the blood smears of about one fifth of the cases, the picture of true plasma-cell leukemia is a rare occurrence and is found in only 1 of every 50 patients with multiple myeloma. Thrombocytopenia is found in approximately one fourth of the cases.

A rapid erythrocyte sedimentation rate is present in far the greater majority of cases and is commonly associated with hyperglobulinemia Marked rouleaux formation and auto-agglutination of red cells due to the excess of gamma globulins may be quite striking and present considerable difficulties in cross-matching unless the matching is done at 28° C.

Frequently myelomatous patients show a marked tendency to bleeding. At times this can be attributed to thrombocytopenia, but in the majority of cases the cause remains unknown In rare instances skin ecchymoses have been caused by the deposition of paramyloid in small cutaneous blood vessels Hemorrhagic tendency may be due to the presence of cryoglobulinemia. Cryoglobulins are globulins that precipitate in the cold and redissolve at 37° C. In cold weather the skin temperature of a patient with cryoglobulinemia decreases far enough to cause precipitation of the cryoglobulinemia in the surface vessels. This is an additional reason why in patients with cryoglobulinemia hemorrhages and superficial necroses develop easily.

Blood Chemistry

The serum calcium is increased in more than 50 per cent of the patients with myelomatosis, probably secondary to rapid absorption of bone substance. Values as high as 17 mg. per cent have been observed. In contrast with the findings in hyperparathyroidism with bone lesions, the serum phosphorus is normal or elevated. The latter occurs, if, as is so frequently the case in multiple myeloma, there is associated renal insufficiency. Then the blood-urea nitrogen and creatinine also are increased. Since the myelomas are purely osteolytic lesions without any osteoblastic proliferation, the level of alkaline phosphatase of the serum remains normal High alkaline phosphatase is seen occasionally in myeloma patients treated with urethane, due to the liver damage, which may develop during long-standing administration of this drug.[25] The frequent hypercalcemia often causes a so-called hypercalcemic syndrome, and metastatic calcification also is present occasionally. In one series of 27 myeloma autopsies, metastatic calcification was found in 10 cases; 2 patients had renal stones.[7]

The uric acid of the serum frequently is elevated, even in the absence of renal failure. This undoubtedly is due to the abnormal proliferation and destruction of the nuclei of the myeloma cells. The hyperuricemia may be the reason for the exceptional cases of gout seen in patients with multiple myeloma.[6]

Solitary and Multiple Plasmocytomas

The presence of a solitary myeloma should be considered only in the absence of Bence Jones proteinuria, hyperglobulinemia and abnormal plasma-cell proliferation in the bone marrow of the rest of the skeleton. The absence of myeloma proteins in urine and serum must be confirmed by electrophoretic examination. Such cases are rare, and, in most instances of so-called solitary plasmocytoma, evidence of generalization of the myelomatosis can be found in the form of one or more of the enumerated abnormalities.

Extramedullary plasmocytomas may occur without a bony component. These usually are present in the mucous membranes of the respiratory tract and rarely in the gastrointestinal tract. In many instances typical myelomatous dissemination develops later.

DIAGNOSIS

In establishing the diagnosis of multiple myeloma, only the presence of Bence Jones proteinuria, myeloma-cell proliferation on bone-marrow aspiration and the typical electrophoretic patterns in serum and urine are pathognomonic.

Multiple myeloma may be confused with almost all the metabolic and the neoplastic diseases of bone. It has already been mentioned that the absence of hypophosphatemia and of an increase of the alkaline phosphatase of the serum distinguishes myeloma from hyperparathyroidism In osteomalacia, hypercalcemia does not occur, and increase of the alkaline phosphatase is a constant phenomenon. Osteoporosis is excluded by the finding of hyperglobulinemia, Bence Jones proteinuria and/or myeloma cells in the marrow aspirate. The roentgenograms of the vertebral column in multiple myeloma and in postmenopausal osteoporosis may be very similar; however, in the latter disease the absorption of bone is limited to spine, ribs and pelvis; in multiple myeloma any part of the skeleton may be involved. The presence of bony proliferation, as seen usually in metastatic disease of bone, militates against the diagnosis of multiple myeloma. Nevertheless, considerable confusion may arise with metastatic carcinoma, lipoid granulomas, lymphoblastoma, bone sarcoma and giant-cell tumors. The last-named neoplasm is allegedly rare in flat bones. Ultimately a biopsy often will be required to settle the diagnostic problem.

The presence of renal insufficiency with "heavy proteinuria" in the absence of hypertension should always suggest the presence of multiple myeloma or of amyloid disease of the kidney. Since uremia in myeloma is associated nearly constantly with the elimination of Bence Jones protein or other myeloma proteins, examination of the urine of uremic patients usually is sufficient to prove or exclude the presence of multiple myeloma. In doubtful cases bone-marrow aspiration must be done. Macroglossia or other localizations of paramyloid always warrant a careful search for the presence of multiple myeloma. Gingival biopsy may show the presence of perivascular amyloid infiltrations. Primary amyloidosis without myelomatosis does occur but is a *rarity*.

In agranulocytosis, Hodgkin's disease, hypersensitivity reactions, *lymphopathia venereum* and all other diseases with hyperglobulinemia, plasmocytosis of the bone marrow often is present. In these cases the plasma cells usually are mature and lack the characteristics of the myeloma cells which have been described before. Occasionally, however, one may have great difficulty in excluding the diagnosis of multiple myeloma. Roentgenologic bone survey, electrophoretic determination of serum proteins and a search for Bence Jones protein in the urine usually will serve to arrive at the correct diagnosis.

REFERENCES

1. Bayrd, E. D.: Bone marrow; on sternal aspiration in multiple myeloma, Blood 3:987, 1948.
2. ———: Long survival in multiple mye-

loma, M. Clin. North America 40:1162, 1956.
3. Bessis, M.: Cytology of the Blood and Blood Forming Organs, New York, Grune, 1956.
4. Block, W. D., Ruckavina, J. G., and Curtis, A. C.: Serum electrophoretic studies on patients with familial primary systemic amyloidosis, J. Lab. & Clin Med. 47:357, 1956; Ultracentrifugal analysis of serum lipoproteins in familial primary systemic amyloidosis, J. Lab. & Clin. Med. 47:365, 1956.
5. Bluefarb, S. M.: Cutaneous manifestations of multiple myeloma, A.M A. Arch. Dermat. & Syph. 72:506, 1955.
6. Bronsky, D, and Bernstein, A.: Acute gout secondary to multiple myeloma, Ann. Int. Med. 41:820, 1954.
7. Carson, C. P., Ackerman, L. V., and Maltby, J. D.: Plasma cell myeloma, a clinical, pathologic and roentgenologic review of 90 cases, Am. J. Clin. Path. 25: 849, 1955.
8. Crow, R. S.: Peripheral neuritis in myelomatosis, Brit. M. J. 2:802, 1956.
9. Freedland, M. S.: Multiple myeloma; a case diagnosis without x-ray evidence of bone lesions, California Med. 84:354, 1956.
10. Goltz, R. W.: Systematized amyloidosis; review of skin and mucous membrane lesions and report of two cases, Medicine 31:381, 1952.
11. Gunnar, R. M., Dillon, R. F., Wallyn, R. J., and Eliasberg, E. I.. The physiologic and clinical similarity between primary amyloid of the heart and constrictive pericarditis, Circulation 12:827, 1955.
12 Heiser, S., and Schwartzman, J. J.: Variations in roentgen appearance of skeletal system in myeloma, Radiology 58:178, 1952.
13. Hino, S.: Plasmocytic myelomatosis in Japan; survey of the literature and report of three cases, Bull. Tokyo M. & Dent. Univ. 2:217, 1956
14. Lawson, H. A., Stuart, C A., Paull, A. M., Phillips, A. M., and Phillips, R. W.: Observations on the antibody content of blood in patients with multiple myeloma, New England J Med. 252:13, 1955.
15. Marks, J.: Antibody formation in myelomatosis, J. Clin. Path. 6:62, 1953.
16. Melicow, M. M., and Cahill, G. F.: Plasmocytoma (multiple myeloma) of testis; report of four cases and review of literature, J. Urol. 71:103, 1954.
17. Nadau, L. A., Megalini, S. I., and Stefanini, M.: Familial multiple myeloma, A.M.A. Arch. Path. 61:101, 1956.
18. Oliver, J.: New directions in renal morphology; a method, its results and its future, Harvey Lect. 40:102, 1944-45.
19. Osserman, E. F., and Lawlor, D. P.: Preliminary observations on difference in carbohydrate binding between abnormal serum and urine proteins of multiple myeloma, Science 120:715, 1954.
20. ———: Abnormal serum and urine proteins in 35 cases of multiple myeloma, as studied by filter paper electrophoresis, Am. J. Med. 18:462, 1955.
21. Perloff, J.: Some unusual cutaneous, cardiac and gastrointestinal manifestations of systematized amyloidosis associated with multiple myeloma, J. Mt. Sinai Hosp. 21:67, 1954-55.
22. Pobanz, D. M., Condon, J. V., and Baker, L. A.: Plasma cell myelomatosis, A.M.A. Arch. Int. Med. 96:828, 1955.
23. Rundles, R. W., and Reeves, R J.: Multiple myeloma—variability of roentgen appearance and effect of urethane therapy on skeletal disease, Am. J. Roentgenol. 64: 799, 1950.
24. Schmorl, G., and Junghanns, H.: Die gesunde und kranke Wirbelsäule in Roentgenbild und Klinik, ed. 2, Stuttgart, Thieme, 1951.
25 Snapper, I, Turner, L. B., and Moscovitz, H. L.. Multiple Myeloma, New York, Grune, 1953.
26. Stich, M. H., Swiller, A. I., and Morrison, M.: The grape cell of multiple myeloma, Am. J. Clin. Path 25:601, 1955.
27. Wallerstein, R. S.: Multiple myeloma without demonstrable bone lesions, Am. J. Med. 10:325, 1951.
28. Wang, C. W., and Robbins, L. L.: Amyloid disease; its roentgen manifestations, Radiology 60:489, 1956.

Myeloma Multiple

Summario in Interlingua

Myeloma multiple es un proliferation de immatur cellulas plasmatic, specialmente in le medulla ossee, partialmente in hepate, splen, e nodulos lymphatic, rarmente in membranas mucose e pelle. In le majoritate del casos, le juvene plasmoblastos remane intra le medulla ossee. In certe casos, grande numeros de cellulas plasmatic appare in le sanguine peripheric, e le diagnose de leucemia a cellulas plasmatic debe esser formulate.

Le morbo es characterisate per tres anormalitates in le metabolismo proteinic.

1. Elimination de proteina de Bence Jones in le urina. Iste proteina se precipita inter 45 e 60 C. Illo se dissolve a 95 C.

2. Augmento del globulinas seral que manifesta in le analyse electrophoretic un configuration characteristic con un altissime e acute picco a base de restringite largor.

3. Primari amyloidosis o paramyloidosis, deponite specialmente in le fibras muscular del corde, del lingua, del larynge, del vias gastrointestinal, e del subcute.

Le examine roentgenologic revela un generalisate resorption de osso, causate per le destruction de trabeculas ossee per le cellulas myelomatic. In plus, le proliferation tumoroide de cellulas plasmatic (plasmocytomas) se manifesta como perforate lesiones osteolytic sin proliferation ossee. Proque neoformation de osso es absente, le phosphatase alcalin del sero non es augmentate. Le constatation de hypercalcemia es frequente. Uremia es un occurrentia frequente in patientes con proteinuria de Bence Jones.

10

Some Effects of X-rays on Bone*

HELEN QUINCY WOODARD, PH.D.

INTRODUCTION

It is generally agreed among radiobiologists that the effect of ionizing radiation on living tissue is almost always deleterious. An apparent exception is the occasional induction of a favorable mutation, but it must be remembered that the lethal or otherwise undesirable mutations induced by radiation outnumber the favorable ones by many orders of magnitude. Other apparent exceptions are the increased activities of enzymes sometimes observed in irradiated tissues Further studies have always shown that such cases do not represent a true stimulation of the system under observation but, rather, a displacement of equilibrium due to greater damage to an opposing, more sensitive system The most striking example of such a displacement of equilibrium is afforded by the whole field of the radiation therapy of cancer. Although cancerous lesions heal after successful radiation therapy, the radiation does not stimulate healing. It permits healing because most cancerous tissue is more readily damaged than is the surrounding normal tissue. When both are irradiated both are injured, but the reparative capacity of the normal tissue is injured less by well-planned radiation therapy than is the growth capacity of the cancer. The end-result is that the neoplastic cells, while they may not all have been killed by the radiation, have been so devitalized that they are walled off or replaced by nonneoplastic cells.

Normal tissues differ greatly in susceptibility to radiation injury, the lymph nodes, the gonads and the intestinal mucosa being among the most sensitive, while muscle is rather resistant. In terms of susceptibility to death from a given amount of radiation energy absorbed, adult bone is not very sensitive, but it is peculiarly liable to injury from therapeutic irradiation because of its high calcium and phosphorus content, which causes it to absorb considerably more energy from a given beam of x-rays than does soft tissue. When X or gamma rays impinge on matter, they react with the atoms of the matter, giving up energy with the emission of secondary electrons. These electrons in turn react with other atoms, producing chemical changes which are the basis of the biologic effects of radiation. The process continues in a succession of steps until all the original electromagnetic energy is transferred to the atoms of the matter The process is a complex one and depends on the potential of the incident radiation and on the atomic number of the atoms encountered. Thus, the intensity of a beam of x-rays generated at 100 kilovolts (K.V) is

---

* From the Biochemistry Department, Memorial Hospital, and the Division of Experimental Surgery, Sloan-Kettering Institute, 444 East 68th St, New York 21, New York

The author is indebted to members of the Bone Service, under Dr B. L Coley, and to members of the Radiation Therapy Department, under Dr J. J Nickson, for their co-operation in making possible the clinical studies reported in this chapter The experimental work was supported in part by a grant from the United States Atomic Energy Commission.

reduced by 80 per cent to 90 per cent after passing through 5 cm. of soft tissue or material of similar composition, while the intensity of million volt x-rays is reduced by only 5 per cent to 20 per cent under the same conditions. If the x-rays fall on bone, the energy absorbed per gram or per centimeter of depth is greater than in soft tissue, and the difference is more pronounced with low-voltage x-rays than with x-rays generated at 1 million volts.

Radiation dosage is commonly expressed in roentgens (r). The roentgen is a unit of measurement that depends on the ionization produced in air under standard conditions. Since the mean atomic numbers of air, water and muscle are nearly the same, dose readings obtained by immersing air ionization chambers in water or tissue-equivalent organic material give a good measure of the dose that would be received by soft tissue under similar conditions during radiation therapy. Depth-dose tables obtained by such measurements are available in standard handbooks.[5] Such tables, however, are not applicable to the calculation of dosage in bone because of its high mean atomic number.

In 1946 Spiers[9] measured the absorption of x-rays of various types in human cortical bone and found that the bone absorbed about 50 per cent more energy per r of million volt x-rays than did muscle, and nearly nine times as much energy per r of 80 K.V. x-rays as muscle. Later, Spiers[10] and Wilson[13] pointed out that much of this energy was dissipated in the bone salt and would not be expected to have any biologic significance. Biologic damage could be caused by that portion of the secondary electrons originating in the bone salt which are scattered into adjacent soft tissues. Since the range of these electrons depends on the voltage of the original x-rays, soft-tissue structures of different sizes should be affected differently by x-rays of different qualities. These authors calculated the energy absorption to be expected in soft-tissue masses of various sizes embedded in, or adjacent to, bone salt. The author of this chapter, working with Spiers,[16] tested this hypothesis by measuring the loss of alakline phosphatase in irradiated mouse bone. Since the size of the phosphatase-bearing areas is known from histochemical preparations, it was possible to calculate the energy absorption to be expected in them. A good correspondence was found between the energy absorption to be expected and the phosphatase loss observed, so that the validity of the hypothesis may be considered to be established.

The figures obtained in this work with

Rough Approximation of the Doses Which May Be Expected in Some of the Structures in Human Bone—Obtained from the Calculations of Spiers and of Wilson

Structure	Size in Microns	Energy Absorption/cc./r in Structure / Energy Absorption/cc./r in Massive Soft Tissue		
		100 kvp x-rays	*200 kvp x-rays*	*1000 kvp x-rays*
Bone solid	——	9.0	5.0	1.5
Canaliculi	1 μ diameter	6.0	2.3	1.2
Lacunae and small vessels	10-50 μ diameter	2.9	1.8	1.1
Haversian canal	100 μ diameter			
Walls		4.5	3.0	1.4
Center		1.0	1.0	1.1

mice cannot be applied directly to human bone because of the differences in the sizes and the degrees of mineralization of the structures involved. The table on page 119 gives a very rough approximation of the doses which may be expected in some of the structures in human bone, as obtained from the calculations of Spiers and of Wilson. It is evident from this table that it is very difficult to make any reliable estimate of the x-ray dose in bone as a whole. The situation is complicated further by the fact that, by the time radiation reaches a deep-seated bone such as the femur, it will have undergone considerable change in quality through interaction with the overlying soft tissue. In addition, the deeper layers of bone may be shielded to an appreciable extent by the more superficial layers. It is perhaps fair to assume that the dose to the sensitive areas in bone from 200 K.V. to 250 K.V. x-rays is likely to be about twice what would be expected from the conventional depth-dose tables, while the dose from 1 million volt x-rays or from the gamma rays of radium or cobalt-60 may be 10 per cent to 30 per cent higher than indicated. Energy absorption in bone from x-rays generated at voltages from 2 million up to about 25 million is slightly higher than at 1 million volts, but the difference is not great enough to be important clinically.

In view of the above uncertainties in calculating energy absorption in bone, it has seemed best, in the remainder of this chapter, to use as the dose to bone the dose which would have been received by soft tissue in the same position as the bone. It must always be remembered, however, that the actual dose absorbed by the bone was higher than the stated figure by an unknown but significant amount

NATURE OF RADIATION DAMAGE TO BONE

The results of numerous experimental studies and clinical observations indicate that radiation damages both the anabolic and the catabolic processes in bone and that the ultimate manifestation of damage, short of complete devitalization, depends on which process is damaged more. Whichever type of damage predominates, the visible evidences of it usually develop very slowly. The slow appearance of evidence of damage is commonly attributed to a naturally slow metabolic rate, but this is not strictly true. Metabolism at trabecular surfaces and in the lumens of young haversian systems is actually quite brisk; as is indicated, for example, by the exceedingly rapid response to parathyroid hormone. The over-all metabolism appears slow because a very large proportion of bone substance consists of crystals of calcium salts embedded in an acellular organic matrix. Where these materials are adjacent to bone cells they are continually built up and removed at a rapid rate.[3] The portion of bone substance which is remote from blood vessels and active cells, on the other hand, is turned over very slowly. Hence, while the first clinical evidence of radiation damage to soft tissue usually appears in days or weeks, evidence of damage to bone of comparable severity may require months or years to become manifest.

In human bone the first clinical evidence of radiation damage is usually a loss in density, as seen in the roentgenograms. This may be generalized, with little alteration in texture, or it may be patchy, areas of very low density alternating with other areas which appear nearly normal. Islands of greatly increased density sometimes appear. They resemble those seen in caisson disease and are probably caused in both cases by necrosis of bone tissue distal to points of obliteration of nutrient vessels. Spontaneous fractures are common in irradiated bones, usually occurring from 8 months to 3 years after exposure. Nonunion is common, but many such fractures heal satisfactorily. A very serious, but fortunately rare, late effect of radiation is the induction of osteogenic sarcoma. If this is due to internally deposited radioactive isotopes rather than to ex-

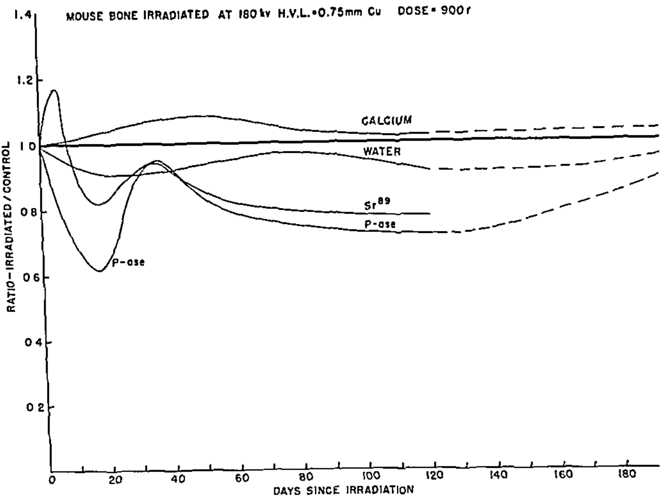


FIG. 1. Changes in the alkaline phosphatase activity, calcium and water content, and radiostrontium uptake in the leg bones of mice at various times after a dose of 900 r of 180 K.V. x-rays. All measurements are expressed as the ratio of the substance in the irradiated bone to that in the contralateral control bone, calculated as per cent of the wet weight of the specimens.

ternal irradiation, malignant change is likely to be preceded by considerable abnormal bone proliferation in regions which, earlier, had seemed quite atrophic. Some of these clinical changes in human bone will be discussed in more detail later, but their significance will be clearer if experimental data from animals are examined first.

EFFECTS OF RADIATION ON ANIMAL BONE

Figures 1 and 2 summarize the results of some work by the author on effects of x-rays on mouse bone. In this work the distal femur and the proximal tibia of each of a series of 20 Gm. male mice were irradiated, the remainder of the animal being shielded. At varying times after irradiation the mice were killed, the irradiated and the contralateral control bones were dissected out, and the alkaline phosphatase activity and the calcium and water contents were determined. The technic is described in detail elsewhere.[16] In some animals about 5 microcuries of radioactive strontium was injected intraperitoneally 3 days before sacrifice, and the strontium uptake in the irradiated and the control bones was determined. Because the epiphyses of mice do not close until old age, if at all, the alkaline phosphatase activity of the bones remains high enough for satisfactory measurement for at least a year. In these experiments it was known that the energy absorption in the phosphatase-bearing

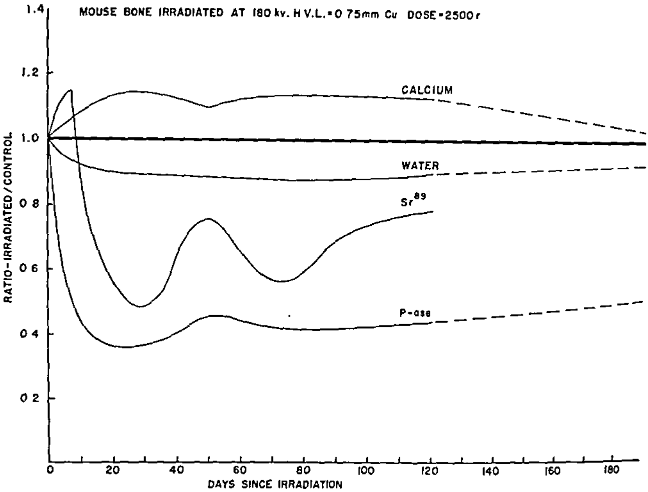


FIG. 2 Same as Figure 1, except that the dose was 2,500 r.

areas in the bones was about 40 per cent greater than it would have been in similar areas in massive soft tissue. Other work showed that the preformed phosphatase was not affected by doses of 20,000 r; hence, the loss in phosphatase activity observed was due to impairment of production of enzyme by the damaged tissue.

Following irradiation there is a prompt depression in phosphatase activity to a minimum, which is reached in 18 to 30 days. After this there is a partial recovery, which is maximal in 30 to 50 days, and is followed by a second depression. The times and the magnitudes of these changes depend on the x-ray dose. The rather scanty data shown by the dotted lines in the charts indicate that recovery is still incomplete at 6 months, and a later series of observations shows that there is evidence of residual damage 1 year after exposure to even 900 r. As 1 year is nearly half the normal life span of the mouse, it is clear that radiation changes are quite persistent.

Alkaline phosphatase takes part in the process of mineralization of bone, although the exact mechanism by which it does so is not entirely clear. Under the conditions of the experiments reported here, mineralization, as indicated by the ability of the irradiated bones to fix radioactive strontium, was not injured as greatly as was their ability to elaborate phosphatase; but the cycles of depression and recovery were closely parallel. Similar results have been reported by Cohn and Gong[3] for phosphatase activity and radioactive calcium uptake in irradiated rat bone, and by Wilson[14] for radioactive phosphorus uptake in mouse bone

The production of alkaline phosphatase and the uptake of phosphate and of calcium and its metabolic analogues are anabolic

processes which are part of the formation of new bone and the replacement of old. The catabolic process of bone resorption or remodeling is difficult to measure quantitatively, but there is indirect evidence that this, also, is damaged by irradiation. In Figures 1 and 2 there are curves representing the change in the ratios of the calcium contents as expressed as per cent of the wet weight of the specimens, of the irradiated and control bones. In view of the fall in alkaline phosphatase and in strontium uptake, it was expected that the calcium content would decrease following irradiation, but, as may be seen from the curves, it appears to rise. This increase is only apparent, however, since the water content falls, so that the calcium, if expressed as per cent of dry weight, shows no significant change. Other experiments showed that the protein content of the specimens decreased in parallel with the loss of water, indicating that a part of the actively metabolizing tissue was lost while the mineral elements were spared. The findings of Cohn and Gong are similar to these, and even more clear cut.

While irradiation can kill bone and dead bone can persist apparently unchanged in the body for long periods, these irradiated bones are not dead. The fact that they remain densely calcified for months, during which their calcifying mechanism is known to be partly inactivated, is rather good evidence that the resorptive mechanism also is severely damaged. The balance between the two processes appears to be different in human and in rodent bones, so that demineralization usually is predominant in the human, but not in mice and rats However, it must be remembered that these animal bones received a single dose of x-rays administered in a few minutes, while human therapeutic irradiation usually is given in divided doses over a period of days or weeks. It is possible that the difference in dose rate, rather than an inherent species difference, is responsible for the difference in the character of the response.

It is evident from the shape of the curves in Figures 1 and 2 that damage and recovery appear in a rhythmic fashion in mouse bone. Several possible explanations of this phenomenon suggest themselves, but, as they have not been proved, it is not profitable to discuss them. In human bone, evidence of damage rests on clinical observations which are not sufficiently precise for the demonstration of the presence or the absence of a periodic response.

EFFECTS OF RADIATION ON HUMAN BONE

Perhaps the most conspicuous clinical aspect of the effects of radiation on human bone is the tardiness with which evidence of damage appears. This complicates greatly the problem of diagnosis, since the patient may be lost to follow-up by the physician who administered the radiation and appear years later in an orthopaedic clinic with bone lesions of a highly equivocal nature. For this reason the orthopaedist always should be alert to anything in the history suggestive of previous radiation therapy and to evidence of radiation damage in the skin. Even when a clear history of radiation treatment can be obtained, often it is difficult to obtain any statement of the dose. In such cases the condition of overlying soft parts is important In general, if there are marked pigmentation and telangiectasia of the skin, palpable fibrosis of muscle and loss of subcutaneous fat, the dose of radiation probably was sufficient to cause changes in a bone situated not more than 5 cm. below the surface There are many exceptions to this relationship, which is influenced by the type of radiation employed and the method of administration, but, in default of an adequate history, it affords a useful clinical guide.

Even when the administered dose is known, it is difficult to predict the amount of damage which is likely to result. This is partly because the energy absorption in bone is not known accurately for the reasons discussed earlier, partly because the method



FIGS. 3-6, Case 1. Fig. 3 *(above)* May 21, 1947· showing "fatigue" type of fracture 16 months after pelvic irradiation for carcinoma of the cervix.



FIG. 4. June 18, 1947: the fracture is larger, but callus is beginning to form.

of administering the radiation (dose rate, etc.) probably affects the response, and partly because minor damage, especially to non-weight-bearing bones, may never be apparent clinically. In an earlier work[15] the author estimated that, for 200 K.V. to 250 x-rays administered at a rate of 200 r to 300 r per day, a cumulative dose of less than 2,000 r had no demonstrable effect on the bones of young adults, while doses of 3,000 r to 4,000 r usually caused definite and sometimes serious damage, and doses greater than 5,000 r were likely to kill the bone. In old people the dose required to produce a particular effect may be somewhat smaller, probably because the already poor circulation is compromised further by fibrosis of soft parts The bones of children, on the other hand, may remain viable after doses of 7,000 r, but relatively small doses to the epiphyses produce severe stunting. Additional data obtained since these figures were published tend to confirm the conclusions quoted.

The earliest change seen in irradiated bone is likely to be an over-all loss of density or a patchy demineralization. This may be associated with mild symptoms, or it may be observed first on roentgenograms taken for unrelated reasons. These changes may disappear later, or they may progress. They sometimes resemble the changes associated with atrophy of disuse; and, in fact, poor function in the shoulder girdle on the side of a radical mastectomy, for example, may contribute to the alteration in texture of the bones in the irradiated field. Unfortunately, radiation changes often resemble the lesions caused by metastases in bone. As substantial doses of radiation seldom are given except for malignant disease, the subsequent appearance of bony metastases is very probable, so that radiation changes which are not of great clinical importance in themselves may be attributed erroneously to disseminated cancer. In cases such as this an open biopsy of the bone may be necessary to establish the diagnosis.



FIG. 5. November 17, 1948: the fracture has united.



FIG. 6. March 22, 1950: trabecular structure is re-established across the fracture line.

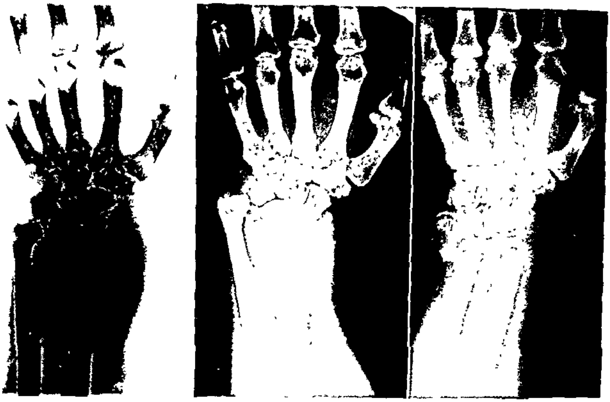
Probably the most important aspect of radiation damage to bone is the occurrence of fractures after trivial injury. These appear most commonly between eight months and three years after exposure. It is difficult to estimate their true incidence, as they are usually of the "fatigue" type and may not be detected. In a series of patients who had received postoperative radiation therapy after radical mastectomy and had unusually full roentgenographic coverage in a special clinic at Memorial Hospital, a number of rib fractures were discovered which had caused minimal symptoms. Most of them were seen in patients who had been treated by methods, now outmoded, which permitted "hot spots" at points where adjacent radiation fields overlapped. Such fractures are not disabling, but they may be serious because of the danger of their being mistaken for metastases. They may be expected to be less frequent following the improved methods of irradiation now in use.

Clinically, the most important type of fracture is that which occurs in the femoral neck following treatment of carcinoma of the rectum, the bladder or the uterine cervix. In the past the incidence seems to have been about 1 per cent. Several excellent studies of this complication have been published,[7,8,11] and only a single typical example will be reported here.

Case 1. A white female, 67 years of age, was treated for carcinoma of the cervix in the winter of 1945-46. Between November 13 and December 13, 1945, she received radiation at 200 K.V., 70 cm. T.S D., to large anterior, posterior, right and left lateral pelvic fields. The dose to the neck of the right femur from the right lateral field was about 1,200 r, and from the other fields a maximum of 1,000 r, with considerable uncertainty as to the exact angle of the fields.

From November 23 to December 28 the patient was treated with a 3-cm. vaginal cone at 130 K.V., 25 cm. T.S D. This may have contributed 500 r to the dose to the right femoral neck. On January 1, 1946, she received intracavitary radium, which may have added another 300 r to the bone dose. Thus, the maximum dose to the femoral neck in 6 weeks was 3,000 r, with 2,500 r as a more probable figure.

In April, 1947, or 15 months after the last irradiation, the patient began to complain of pain in the right hip. This increased until, on May 21, 1947, a roentgenogram was taken which showed an incomplete "fatigue" type fracture of the femoral neck (Fig. 3). This increased



FIGS 7-9, Case 2. Fig. 7 *(left)* June 22, 1931: giant-cell tumor of the left radius 2 months after an x-ray dose of 4,400 r. The ulna is normal except for pressure changes.

FIG. 8 *(center)* May 11, 1932: after an additional x-ray dose of 2,500 r. There has been no bone regeneration in the radius The ulna still appears to be normal.

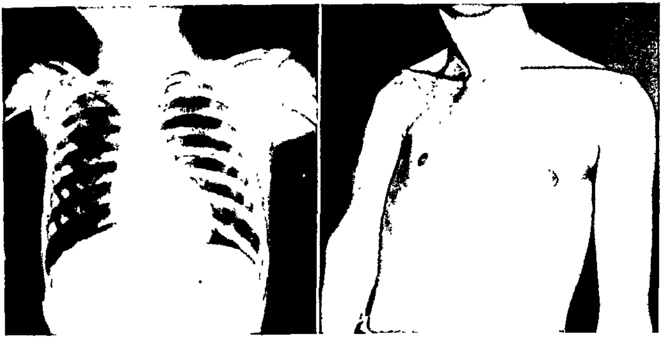
FIG 9 *(right)* January 26, 1946. the ulna has disintegrated as a result of the irradiation 14 years previously. (Coley, B. L.: Neoplasms of Bone, New York, Hoeber)

slightly during the next month but also showed some evidence of callus formation (Fig. 4). The patient was allowed to walk with crutches without weight-bearing, and by November 17, 1948 [illegible] lished across the fracture line, and the patient was symptom free except for 3 cm. of shortening. She still was well at the last examination, 10 years after irradiation.

This case is presented to illustrate the gradual development and the incomplete nature of many radiation-induced fractures. The dose was sufficient to cause temporary reduction of the regenerative capacity of the bone below that necessary to repair ordinary wear and tear, but it was not sufficient to prevent eventual recovery, even in an elderly woman. As a large part of the dose to the upper femur comes from the lateral fields, such fields now are used in pelvic irradiation only in exceptional circumstances; hence, postirradiation fractures may be expected to be less frequent in the future. While they constitute a serious complication, the possibility of their occurrence is not to be considered as a contraindication to well-planned pelvic irradiation, but rather as a calculated risk inherent in a lifesaving therapeutic procedure.

The next case illustrates the results of gross overirradiation of a benign tumor *during the early days of radiation therapy*, with incidental destruction of a normal bone included in the field

Case 2. A 40-year-old white male was treated at another hospital in March and April, *1931*, for a giant-cell tumor of the left radius. The tumor dose is thought to have been about 4,400 r. Figure 7 illustrates the appearance of



FIGS. 10 & 11, Case 3. Fig. 10 *(left)* April 16, 1941: showing stunting of the bones of the right shoulder 5 years after an x-ray dose of between 6,000 r and 8,000 r. Fig. 11 *(right)* November 19, 1947: showing appearance 12 years after treatment.

the lesion in June, 1931. It will be noted that the ulna looks normal except for pressure changes, and that the cortex of the radius cannot be seen, although some cortical bone usually is evident about even advanced giant-cell tumors.

The patient was observed for a time at Memorial Hospital, but there was no evidence of healing. On the assumption that this was due to continuing tumor activity, he was given additional therapy at intervals from September, 1931, to February, 1932, for a tumor dose of 2,500 r at 130 K.V., 40 cm. T.S.D.

The appearance in May, 1932, is shown in Figure 8. Here the tumor has regressed without recalcification, and the resultant shortening has led to dislocation of the ulna. Wrist function was poor, but improved following the complete disintegration of the ulna, with the formation of a pseudarthrosis The condition in January, 1946, 14 years after the last irradiation, is shown in Figure 9.

In this case the dose was so large that it not only destroyed the tumor but prevented any regeneration in such fragments of uninvolved bone as may have remained in the radius, and destroyed the previously normal ulna.

As is well known, the irradiation of young bone may result in marked retardation of growth. The minimum dose for stunting in young rats has been reported[6] to be 500 r, and 600 r has been found[12] to retard the growth of the forelegs of puppies. In the very small series of children observed by the author it appears that 1,200 r will cause measurable but not severe stunting, and doses in the neighborhood of 4,000 r will have a marked effect. The effect of very large doses is illustrated in the following case:

Case 3. A white 18-month-old male when first admitted to Memorial Hospital in December, 1934, had a tumor of the right clavicle which was diagnosed on biopsy as Ewing's endothelioma of bone. During the next 17 months he received four courses of x-ray therapy at 200 K.V., 50 cm T.S.D., or a total tumor dose of 7,800 r. The dose to the scapula and the upper humerus was somewhat smaller, but can hardly have been less than 6,000 r. The tumor in the scapula regressed and had not recurred when the patient was last seen on July 2, 1956.

Retardation of growth of the irradiated shoulder was well marked 3 years after the last treatment, and the discrepancy between the two shoulders continued to increase until general body growth was complete.

The appearance of the bones on April 16,

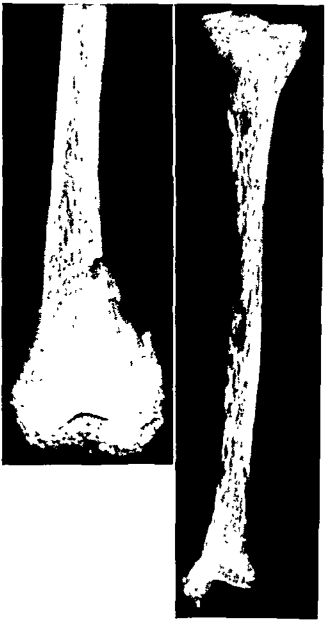


FIG. 12 Roentgenograms of dissected amputated specimen, showing an osteogenic sarcoma of the femur and extensive radiation changes in the tibia caused by radium deposited 37 years previously. (Woodard, H. Q. Cancer, vol 10, frontispiece)

1941, 5 years after the end of therapy, is shown in Figure 10. The irradiated bones are small, poorly mineralized and somewhat irregular in texture. The external appearance of the patient on November 19, 1947, 12 years after treatment, is shown in Figure 11. Changes in the skin had become conspicuous for the first time shortly before this picture was taken.

It will be noted that the irradiated shoulder, while very small for a youth 15 years of age, is considerably larger than that of a 2-year-old child. In other words, while growth was greatly retarded, it was not completely abolished even by this large dose of radiation. The risk of changes such as these, while fully justified in treating children with malignant disease, constitutes a contraindication to the use of radiation for benign conditions.

In the nineteen twenties osteogenic sarcoma occurred in a number of women who had ingested small amounts of radium while painting watch dials with luminous paint Since that time it has generally been recognized that internally deposited radioactive substances can induce malignant change in bone. A large amount of experimental work has shown that osteogenic sarcoma can be induced at will in animals of several species by either radium or radioactive strontium. The induction time varied with the dose but usually was a substantial fraction of the natural life span of the animal. The problem in man has been reviewed in an admirable monograph by Aub and others[1] and need not be considered in detail here.

There exist now safety regulations adequate to prevent further mishandling of radium such as that responsible for the injury of the dial painters; hence, it might be supposed that the issue is not of present interest, but, unfortunately, this is not so. An unknown number of people probably are carrying a radium burden acquired through drinking radioactive waters, a form of treatment which was popular 30 years ago. Some of the dial painters are still alive, and one was admitted to Memorial Hospital in 1956 suffering from an osteogenic sarcoma induced by radium ingested 37 years ago and still present in her skeleton. A roentgenogram of the dissected amputated specimen is shown in Figure 12. The tumor arose in the lower femur, crossed the joint space and invaded the upper tibia. The appearance of the lower tibia, which was free of tumor, is

characteristic of the changes produced by radium deposited in bone.

The use of radioactive isotopes is already extensive and is increasing rapidly. The United States Atomic Energy Commission has imposed stringent safety rules for the handling of these substances, so that it is unlikely that their internal deposition as a result of peacetime industrial or laboratory accidents will become a health problem in the future. In atomic warfare, however, all regions of fall-out can be expected to be heavily contaminated with strontium-90. This is a long-lived isotope, is one of the major products of uranium fission, and is metabolized in a manner very similar to that of calcium and radium. It constitutes a hazard of very grave import.

While it has been clear for 30 years that osteogenic sarcoma could be induced by long-continued low-level internal irradiation, it has only recently been clear that external irradiation could produce the same result. In most cases the dose has amounted to several thousand roentgens delivered in a few weeks. These x-ray-induced sarcomas are quite rare. A total of 22 have been seen at Memorial Hospital to date, with induction periods of 4 to 24 years.[4] This is a very small fraction of the entire number of patients who have received radiation therapy and have been followed for comparable intervals. Nevertheless, the hazard, though slight, is definite and warrants careful investigation whenever a patient complains of persistent pain in a previously asymptomatic bone in a region which has been irradiated.

SUMMARY

Because of its high calcium and phosphorus content, bone absorbs more energy from an x-ray beam than does soft tissue.

The results of animal experimentation and of clinical observation indicate that both the anabolic and the catabolic processes in bone are damaged by external irradiation. Similar effects are produced by internally deposited radioactive isotopes

Evidence of radiation damage in bone is slow to appear and is long lasting.

The clinical signs of radiation damage in bone are:

1. Stunting of growth in children
2. Generalized or patchy demineralization with or without contrasting infarcted areas
3. Pathologic fractures, usually of the "fatigue" type, occurring from 8 months to 3 years after exposure.
4. Total disintegration of bone after very heavy exposure
5. Osteogenic sarcoma developing many years after single courses of external irradiation, or after long-continued low-level irradiation from internally deposited radioactive isotopes. This is rare.

REFERENCES

1. Aub, J. C., Evans, R. D., Hempelmann, L. H., and Martland, H. S.: The late effects of internally-deposited radioactive materials in man, Medicine 31:221-329, 1952.
2. Bauer, C. H., Carlsson, A., and Lindquist, B.: Evaluation of accretion, resorption, and exchange reactions in the skeleton, Kungl. Fysiografiska Sallskapets I Forhandlingar 25:1-16, 1955.
3. Cohn, S. H., and Gong, J. K.: Effect of 2000 roentgens local x-irradiation on metabolism and alkaline phosphatase activity of rat bone, Am. J. Physiol. 173:115-119, 1953.
4. Cruz, M., Coley, B. L., and Stewart, F. W.: Post-irradiation bone sarcoma; report of 11 cases, Cancer 10:72-88, 1957.
5. Glasser, O., Quimby, E. H , Taylor, L. S., and Weatherwax, J. L.: Physical Foundations of Radiology, ed 2, New York, Hoeber, 1952.
6. Hinkel, C. L.: The effect of roentgen rays upon the growing long bones of albino rats. I. Quantitative studies of the growth limitation following irradiation, Am. J. Roentgenol 47:439-457, 1942.
7. McCrorie, W. D. C.: Fractures of the femoral neck following pelvic irradiation, Brit. J. Radiol. 23:587-592, 1950.
8. Smith, F. M.: Fracture of the femoral neck as a complication of pelvic irradiation, Am. J. Surg. 87:339-346, 1954.
9. Spiers, F. W.: Effective atomic number and energy absorption in tissues, Brit. J. Radiol. 19:52-63, 1946.

10. ———: The influence of energy absorption and electron range on dosage in irradiated bone, Brit. J. Radiol. 22:521-533, 1949.
11. Stampfli, W. P., and Kerr, H. D.: Fractures of the femoral neck following pelvic irradiation, Am. J. Roentgenol. 57:71-83, 1947.
12. Wilkins, W. E., and Regen, E. M.: The influence of roentgen rays on the growth and phosphatase activity of bone, Radiology 22:674-677, 1934.
13. Wilson, C. W.: Dosage of high voltage radiation within bone and its possible significance for radiation therapy, Brit. J. Radiol. 23:92-100, 1950
14. ———: The uptake of phosphorus 32 by the knee joint and tibia of six-week-old mice and the effect of x-rays upon it; variation of uptake with time after a dose of 2000 r of 200 kv x-rays, Brit. J. Radiol. 29: 86-91, 1956.
15. Woodard, H. Q., and Coley, B. L.: The correlation of tissue dose and clinical response in irradiation of bone tumors and of normal bone, Am. J. Roentgenol 57: 464-471, 1947.
16. Woodard, H. Q, and Spiers, F. W.: The effect of x-rays of different qualities on the alkaline phosphatase of living mouse bone, Brit. J. Radiol. 26:38-46, 1953.

Certe Effectos de Radios X Super le Osso

Summario in Interlingua

Le ossos, possedente un alte contento de calcium e phosphoro, absorbe plus energia ab un fasce de radios X que histos molle.

Resultatos de experimentos animal e de observationes clinic indica que tanto le processos anabolic como etiam le processos catabolic in le osso suffre sub irradiation externe. Simile effectos es producite per depositos interne de isotopos radioactive.

Le manifestationes de lesiones radiational in le ossos appare lentemente. Illos es perdurative.

Le signos clinic de lesion radiational in osso es le sequente:

1. Crescentia atrophic in juveniles

2. Dismineralisation generalisate o discrete, con o sin contrastante areas infarctate.

3. Fracturas pathologic, usualmente del typo a "fatiga," occurrente inter octo menses e tres annos post le exposition.

4. Disintegration total del osso post fortissime expositiones.

5. Sarcoma osteogenic, occurrente multe annos post unic cursos de irradiation externe o post prolongate irradiation a basse nivellos de energia ab depositos interne de isotopos radioactive. Isto es rar.

11

Skeletal Lesions Produced by Aminonitriles

IGNACIO V. PONSETI, M.D.*

Diets containing great amounts of peas of the genus *Lathyrus* induce in man a syndrome called lathyrism, characterized by spastic paraplegia, pain, hypesthesia and paresthesias. Lathyrism has been known to exist since antiquity, and epidemics still occur sporadically in times of famine in India, North Africa and Southern Europe.[24,27] A degeneration of the lateral columns of the spinal cord was found in the only two postmortem examinations reported.[21] No skeletal lesions have been ascertained in patients with lathyrism, although systematic studies of the skeleton are lacking. The peas more commonly blamed for human lathyrism are the chickling vetch *(Lathyrus sativus)*, the flat-podded vetch *(Lathyrus cicera)* and the Spanish vetchling *(Lathyrus clymenum)*.[13,24,29] The nature of the toxic agent present in these peas is unknown. These species of Lathyrus peas apparently are not toxic to rats, whereas in monkeys they induce spastic paralysis and convulsive seizures with degenerative lesions in the spinal cord and the brain.[27] It has been reported that cattle, horses, swine and ducks also are sensitive to these peas.[24] The skeletons of these animals have not been studied.

The occurrence of kyphoscoliosis, exostosis, hernias and lameness of the hind legs in rats fed diets containing sweet-pea *(Lathyrus odoratus)* seed was reported by Geiger, Steenbock and Parsons in 1933.[11] Lewis *et al.*[14,15] in 1948 noted similar deformities in rats fed other species of Lathyrus peas *(Lathyrus hirsutus, Lathyrus tingitanus* and *Lathyrus pusillus)*. These authors suggested that the lameness and the spastic paralysis observed in these animals might be due to cord compression at the site of the kyphosis rather than to a primary neurologic lesion. Vivanco and Jiménez Diaz,[29] on the other hand, thought that the paraplegia in these rats was of neurotoxic origin. Ponseti and Baird[17] studied serial sections of the spinal cord of a group of rats fed *Lathyrus odoratus* seeds; no microscopic changes in the cells or the tracts were observed except at the site of the severe kyphoscoliosis in the rats with paraplegia. At this site the funiculi and the gray matter were greatly distorted, with loss of cells and local loss of myelin in all funiculi. It can be assumed that the paraplegia in these animals is caused by cord compression at the site of the kyphoscoliosis.

Lathyrism in man and lathyrism in the rat thus appear to be two completely different diseases with unrelated pathology and caused by different species of Lathyrus peas. Vivanco and Jiménez Diaz[29] have suggested the term *odoratism* to designate the syndrome that develops in rats fed *Lathyrus odoratus* seeds, thus differentiating this syndrome from human lathyrism.

Recently odoratism has been studied intensively. Ponseti and Baird reported the occurrence of dissecting aneurysm of the aorta in rats fed diets containing *Lathyrus*

* Department of Orthopedic Surgery, State University of Iowa, Iowa City, Iowa

odoratus seeds and described the pathogenesis of the skeletal lesions observed in these animals.[17,19] Dupuy and Lee[9] isolated an active crystalline substance from singletary peas *(Lathyrus pusillus).* Schilling and Strong[23] isolated a similar compound from *Lathyrus odoratus* seeds and characterized it as β-(N-γ-L-glutamyl)-aminopropionitrile. Shortly afterward it was recognized that the active portion of the molecule is β-aminopropionitrile (BAPN).[1,5,30] This compound is present in all the peas that produce odoratism *(Lathyrus odoratus, Lathyrus pusillus* and *Lathyrus hirsutus)* and absent from the peas that cause human lathyrism.[28] It is also absent from the legumes of common consumption in our diets. Two other aminonitriles—aminoacetonitrile (AAN) and methyleneamino-acetonitrile—have been found to be more active than BAPN in the production of the lesions of odoratism in the rats. Another related substance—bis(β-cyanoethyl) amine—fed to rats produces slight skeletal lesions but severe neurologic changes which deserve further investigation. The importance of these studies arises from the similarities observed histologically between the lesions of odoratism in the rat and certain human diseases such as dissecting aneurysm of the aorta and slipping epiphysis.

Aminonitriles fed to rabbits, mice, chicks, frogs and newts have caused lesions resembling odoratism in the rat.[4] The mice are quite resistant to the BAPN, whereas the frogs are resistant to AAN. The action of the aminonitriles is tissue specific, affecting the mesodermal tissues, probably some component of the ground substance. The vertebrates are most sensitive to the aminonitriles during certain periods of growth; they do not appear to be affected during the earlier stages of embryonary development and only slightly when they mature. The actively growing epiphyseal plates and certain tendon and muscle insertions are damaged greatly by the aminonitriles.

Stamler[25] has studied the effect of *Lathyrus odoratus* peas on reproduction in the rat. Mature rats of both sexes maintained on a 50 per cent pea diet remained in good health for several months. The male rats showed active spermatogenesis and no testicle atrophy, even after 8 months of a 50 per cent pea diet. Offspring obtained by mating these males with normal females showed no abnormalities. In the female rat, menstrual cycles were not interrupted, and they mated freely. Conception occurred in a high percentage of matings.

The final few days of gestation constitute the critical period for exhibition of the toxic effect of the pea. Normal litters were born to females on a 50 per cent pea diet during the first 16 days of pregnancy, but giving this diet for one more day resulted in death of almost all fetuses. Giving the diet from the 17th to the 20th day was also highly toxic to the unborn young. Diets containing 20 per cent *Lathyrus odoratus* meal were lethal for the rat fetus if begun by the 17th day of gestation.

Many young were born dead with little evidence of decomposition, while others were feebly alive at birth but succumbed soon afterward. Both living and dead were fragile and hydropic in character. Muscles and connective tissues were poorly developed, and cohesion of various skeletal and connective tissues appeared faulty. Massive hemothorax from aortic rupture was a frequent demonstrable cause of death. Kyphoscoliosis developed in many fetuses Lesions produced by aminonitriles mimicked those produced by the pea diets. Diets containing 0.05 per cent BAPN proved uniformly lethal to fetuses when given beginning the 17th day of pregnancy. AAN caused death of the fetuses at much lower concentrations.

The skeletal lesions which occur in the young rats are studied better by feeding stock diets containing 50 per cent *Lathyrus odoratus* seeds or 0.1 per cent BAPN or 0.025 per cent AAN.[19] The toxicity of these three diets is quite similar. Weanling rats approximately 3 weeks old fed these diets show widening of the epiphyseal plates of



FIG. 1. ... of a 6-we... taining 0.4 ... of age.

... long bo... tologic sectio... great increase ... in size of the cartilage cells, which are not arranged in orderly rows but clustered. They appear separated by thick, deeply metachromatic septi of cartilage matrix, which is somewhat fibrillated. One or two weeks later the cartilage matrix appears to disintegrate, particularly in the plane between the zone of proliferating cells and the calcified cartilage. In that plane a rent often occurs and may extend throughout the entire width of the epiphyseal plate (Fig 1) There may



FIG. 2. Upper tibial epiphyseal plate of a 6-week-old rat fed stock diet containing 0.2 per cent BAPN from 3 weeks of age. Note islands of cartilage cells extending deep into the metaphysis.



FIG. 3. An 8-week-old rabbit fed stock diet containing 0.2 per cent AAN from 6 weeks of age. This rabbit had bilateral complete slipping of the upper humeral epiphyses.

be some hemorrhage at this area. Slipping of the epiphysis occurs along this line of diminished resistance (Figs. 3 & 4).

The calcification of the cartilage adjacent to the metaphysis and the endochondral ossification appear to proceed, although in a disarranged manner. No osteoid seams are seen in the metaphysis. However, in small areas the rows of degenerating cartilage cells appear completely disorganized, the cartilage matrix does not calcify, and, consequently, there is no endochondral ossification at that site. Tongues of cartilage are seen to extend deep into the metaphysis, but there is no abnormal amount of osteoid (Fig. 2).

Local defects of ossification also are responsible for the presence of areas in the metaphysis filled with fibrous tissue. These defects occur in epiphyseal plates with and without slipping. If a slipping of the epiphysis occurs, the periosteum becomes detached from the metaphysis, followed by formation of new periosteal bone at that site. After the epiphysis has slipped, the epiphyseal plate is disorganized and contains abundant fibrous tissue and fibrocartilage. However, in some instances new columns of proliferating cartilage form in the area adjacent to the metaphysis, and bone growth may continue. These epiphyseal plate lesions are more severe in the more actively growing epiphyseal plates, such as the lower end of the femur and the upper end of the tibia. The upper femoral epiphysis slips rarely in rats but commonly in rabbits (Figs. 3 & 4).



FIG. 4. Roentgenogram of an 8-week-old rabbit fed stock diet containing 0.2 per cent AAN from 6 weeks of age. Complete slipping of the right upper femoral epiphysis and partial slipping of both upper humeral epiphyses are present

The older the animal the less extensive are the lesions in the epiphyseal plate for a given period of experimental feeding.

Another lesion of great interest to the orthopaedic surgeon occurs at the site of insertion of ligaments and tendons where the cartilage matrix appears to lose cohesion, and these insertions become loose. The ligaments are partially detached from the underlying bone. Connective tissue appears at the site of the detachment, and later on new bone trabeculae form and usually are lined up along the direction of pull. The earliest changes occur at the digital fossa in the upper femur; in weanling rats fed minimal amounts of aminonitriles, the insertions of the outward rotators of the femur become loose during the first days of the experimental diet, and toward the end of the third week the digital fossa is occupied by a large mass of immature new bone (Fig. 5). The same lesion, but less severe occurs at the insertions of the interspinous, the supraspinous and the costotransverse ligaments of the vertebrae.

Extensive areas of periosteal new bone form over the long bones and the pelvis of weanling rats a few weeks after the start of the aminonitrile diets. The new bone appears to form because of the separation of the periosteum from the underlying bone. Periosteal new bone forms in greater amounts at the site of tendon insertions, such as at the upper third of the femur, where the gluteus maximus and the psoas insert. Large masses of young very cellular connective tissue develop underneath the lifted periosteum. Metachromatic granules and globules are present in the ground substance between the young fibroblasts. New bone trabeculae develop later on in these areas of young connective tissue. Neither inflammatory cells nor an unusual amount of osteoid tissue is seen. Administration of a stock diet containing 0.05 per cent of amino-acetonitrile produces extensive periosteal new bone formation in the femurs and the humeri in 1 week.



FIG. 5. Frontal section of the upper end of the femur of a 42-day-old rat fed a stock diet containing 50 per cent *Lathyrus odoratus* seed from 22 days of age. Periosteal new bone formation and abundant new bone occupying the digital fossa can be seen. The cartilage plate of the greater trochanter is wide.

Kyphoscoliosis develops in young rats fed aminonitriles. Usually the kyphoscoliosis is more severe when diets containing 0.1 or 0.2 per cent of BAPN are administered to 3-week-old rats. The first changes take place at the level of the thoracolumbar junction after the third week of feeding. A kyphosis develops due to a slow forward slipping of the cephalad vertebra over the caudal vertebra. Similar changes occur later on in the mid-thoracic area. The mid-sternal segments angulate and protrude forward. The ribs also become deformed and usually angulate downward. A left thoracolumbar kyphoscoliosis with the apex at the sixth thoracic vertebra is the common deformity (Fig. 6). Well-developed lumbar curves rarely are seen.

Histologic studies of the spine reveal that the vertebral slipping, which causes the sco-



FIG. 6. Roentgenograms of a 13-week-old rat fed a stock diet containing 50 per cent *Lathyrus odoratus* peas from 4 weeks of age. Note scoliosis, thoracic deformity, subluxation of the shoulders and bowing of the long bones.

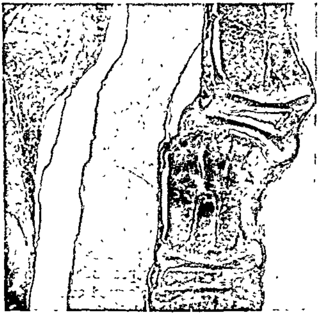


FIG 7 Sagittal section of the midthoracic vertebrae in a 56-day-old rat fed a stock diet containing 0.2 per cent BAPN from 23 days of age. Slipping of one vertebra and loosening of the interspinous ligaments at the level of the slipping can be seen



FIG. 8. Sagittal section of the vertebrae of the thoracolumbar junction of a 53-day-old rat fed a 50 per cent *Lathyrus odoratus* diet from 23 days of age. A slight slipping of the vertebrae with some compression of the spinal cord can be observed.

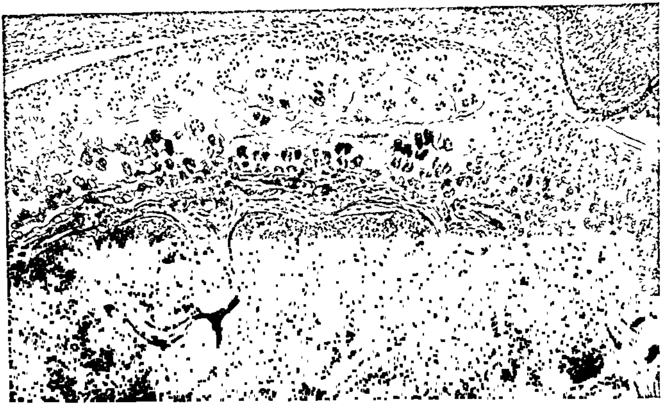


FIG. 9. Photomicrograph of the knee-joint cartilage of a 242-day-old rat fed diet containing 50 per cent *Lathyrus odoratus* seed from 56 days of age.

liosis, occurs at the site of the weakened vertebral epiphyseal plate. However, the loosening of the attachments of the ligaments of the vertebral syndesmosis is a prerequisite for the vertebral slipping (Fig. 7). The slipping produces some detachment of the periosteum from the vertebral body, which is followed by the formation of new periosteal bone. The intervertebral disks do not appear to be abnormal in the young animals, and the annulus fibrosus remains attached to the cartilaginous plate. Slipping usually occurs in only one of the two epiphyseal plates adjacent to an intervertebral disk. In some animals fed diets containing higher doses of aminonitriles, the vertebral slipping may occur rapidly, and one vertebra may be seen to slip completely in front of the vertebra beneath, severing the spinal cord. If the rats are over 1 month old when the experimental feeding is started, the epiphyseal slipping occurs slowly, or not at all. In these cases a complete rent in the epiphyseal plate is not seen, and there is only a minor sliding of the cartilaginous plate over the vertebra, producing a small degree of scoliosis or kyphosis (Fig. 8). In the older rats the kyphotic component of the deformity is found to be much more common than the scoliosis.

The skeleton of these animals is osteoporotic. The osteoporosis may be due to the relative inactivity of the animals when the epiphyseal slipping and the periosteal detachments occur and to malnutrition.

A lesion resembling Osgood-Schlatter disease of human patients is seen in the experimental animals. Areas of softening and hemorrhage develop in the cartilage beneath the tibial tuberosity 4 weeks after the onset of the diet. The tibial tuberosity becomes somewhat loose and fragmented, and often is pulled away from the tibia, to which it still remains attached by fibrous tissue. Occasionally the patella is seen to recede upward along the anterior surface of the femoral shaft. The capsule insertions of the shoulder joint also become loose, and sub-

luxations and dislocations of the shoulders are seen in many animals.

Degenerative arthritis is observed in mature rats fed aminonitriles for several months. The cartilage matrix stains red with eosin in areas deep in the joint cartilage. There is fibrillation of the matrix, and the cartilage cells proliferate and cluster (Fig. 9). Capillaries invade the areas of degenerated cartilage; often this is followed by new bone formation. Circumscribed areas filled with connective tissue are observed in the joint cartilage. The subchondral plate becomes disrupted and irregular, and the underlying bone is sclerotic. Thickening and some hyperemia of the synovial membrane occur. New bone proliferations can be seen at the loosened capsule insertions. Bony spurs also are observed at the margins of the vertebral bodies.

Six rats 2½ years old at the time of death, which occurred after 12 to 16 months on the aminonitrile diets, had in some bones mosaic patterns and cement lines that stained deep blue with hematoxylin. These areas resembled somewhat the bone seen in human patients with Paget's disease.

LESIONS OF SKELETAL MUSCLE, FASCIA AND APONEUROSIS

The experimental animals on diets containing *Lathyrus odoratus* seeds or aminonitriles have a somewhat unsteady and jerky gait which has been described as spastic paralysis Length-tension studies done by Shepard[19] on rats with odoratism point to the absence of spasticity. The poorly coordinated gait that these animals develop may be due to pain following the periosteal detachments, slipping epiphyses or degenerative arthritis, or in some rats it may be due to cord damage produced by the slipped vertebrae Oxygen-consumption analyses of muscles from animals with odoratism showed a higher oxygen consumption than did the control animals Muscle-creatinine determinations on the soleus muscle indicate no difference between the experimental and the control rats. Abdominal and inguinal hernias are fairly common in the experimental animals. Electron microscopic studies of the tail-tendon fibers of experimental animals revealed nothing abnormal in the structure of the collagen fibers. The periodicity of the collagen fibers was the same in experimental animals as in the control animals.

DISSECTING ANEURYSM OF THE AORTA

The production of dissecting aneurysm of the aorta in the rat by feeding diets containing *Lathyrus odoratus* seeds was first reported by us in 1952.[17] The dissecting aneurysm occurs only in rats started on experimental diets shortly after weaning. No aneurysms have been observed when the Lathyrus diet is started after 60 days of age. The rats affected die suddenly usually 5 to 9 weeks after beginning the experimental feeding. At the necropsy a massive bilateral *hemothorax is found. The dissecting* aneurysm occurs usually in the ascending aorta, arch, or in the upper thoracic aorta. We have not observed aneurysms in the abdominal aorta. The lesion occurs when the skeletal deformities still are mild, and it is not due to mechanical distortion of the aorta. Histologic examinations of the aorta show that the elastic fibers separate from each other, perhaps owing to loss of the binding power of the ground substance which holds these fibers together. The intima ruptures at the site of weakening of the media, and blood *penetrates and dissects* between the loosened fibers of the media. The adventitia then may rupture, and blood extravasates, producing hemothorax or hemopericardium. In some rats, dissecting lesions were observed with attempts at repair; very cellular connective tissue patched the defect of the arterial wall. The smaller arteries, veins and capillaries do not appear altered, although no detailed studies have been made of these vessels.

The lungs, liver, spleen and kidneys of

these animals appear normal. The pancreas, pituitary, thyroid, adrenals, prostate gland and testicles also appear to be normal histologically; however, in very old rats fed aminonitriles for over 200 days some degree of testicle atrophy and partial arrest of spermatogenesis may develop. Nothing remarkable was observed in the other endocrine glands.

LATHYRISM IN THE FROG

The larvae of the South African toad, *Xenopus laevis,* fed powdered *Lathyrus odoratus* seeds ad lib. or weak solutions of BAPN develop severe deformities of the limbs if the feeding is started 10 to 12 days before the expected breakthrough of the forelimbs.[4] Treatment of early stages is without apparent effect on limb development. Treatment started after metamorphosis is almost ineffective. BAPN in concentration of 10 μl/liter causes death of the animals during metamorphosis. The limb deformities are most severe, and subcutaneous hemorrhages occur frequently in this group. Metamorphosing tadpoles receiving BAPN at 2 μl/liter show badly twisted extremities in 10 days. These animals complete their metamorphosis, but they are too weak to survive beyond this stage. The knees and the ankle joints are dislocated. A loosening of leg-muscle insertions, tendons and ligaments is noticeable under binocular microscope after removal of the skin. Microscopic examination of animals treated only 5 to 6 days shows wide clefts between cartilage and the covering connective tissue in the region of the joints. This rent formation is the beginning of the lesions in the young toads, a process that eventually results in dislocation of the joints. The cartilage appears normal, and the periosteal ossification seems unaffected. Lesions also develop in the dorsal musculature about 10 days following the onset of the experiments After removal of the dorsal skin of treated tadpoles the intersegmental septa are seen to be abnormally wide. Microscopic examination shows a very loose connective tissue in these septa. The muscle segments are atrophic.

The general body growth of the treated larvae becomes increasingly retarded. Experimental animals are thinner and weaker than the controls, probably because food intake is impaired. The minimal dose producing noticeable effects is less than 0.5 μl/liter. The high potency of AAN in producing skeletal lesions in rats has not been verified in tadpoles. The tadpoles appear to be resistant to this compound.

LATHYRISM IN CHICK EMBRYOS

Incubating hen's eggs were injected with BAPN. At a dosage of 1 μl and more per egg this compound has a lethal effect. The lesions produced in lower dosage groups are highly specific, affecting particularly the development of the legs. Size and weight of the animals are the same as those of the controls. Whether injected on the 4th or the 10th day, a bending of the femur at the lower end of the primary ossification center appears on the 13th day of incubation. No dislocation of joints was observed. Cartilage and bone appear histologically normal.

Studies now are under way in several laboratories in an effort to determine the biochemical basis of the lesions produced by aminonitriles in animals. Histologic examinations give the impression that it is a defect in the formation of the ground substance which is responsible for most of the lesions. It is not known if the chondroitin sulfate moiety of the ground substance or the protein fraction or some other factor is at fault.

The metabolism of sulfur has been studied. Partition of urinary sulfur by rats fed Lathyrus peas in comparison with control rats gave no evidence of altered sulfur metabolism in lathyrism [20]

The deposition of sulfur^{35} in the epiphyseal plates, the bones and the aorta of rats with odoratism was investigated by radioautography.[20] The S^{35} is chiefly in the form of chondroitin sulfate. Radioautographs dem-



FIG. 10 Photomicrograph of a biopsy specimen from the level of the upper femoral epiphyseal plate (×20) of a 13-year-old girl with a slight degree of epiphyseal slipping The epiphyseal plate is very wide, and an extensive cleft is seen extending through the middle.

onstrated deposition of S^{35} in the epiphyseal plates in about equal amounts in experimental and control animals. A high concentration of S^{35} was observed in experimental rats at the site of periosteal detachments overlying areas of new bone formations. The uptake of S^{35} by chondroitin sulfate was the same in experimental as in control animals; therefore, it may be assumed that the sulfur content of the chondroitin sulfate is not altered greatly in odoratism. These findings appear to be in accordance with the work of Bauer *et al.*[2]

It has been reported that diets high in vitamin E, in casein and in gelatin give partial protection from the lesions of lathyrism [1,6,7] These reports have not been corroborated by other authors.[20] Neither vitamin E nor many other antioxidants tried in experimental diets have proved to be of value in delaying the development of skeletal lesions in lathyrism. A possible relationship between vitamin E and the ground substance is not well understood. Rats placed on vitamin E deficient diets for periods of 4 to 7 months developed severe testicular atrophy and muscle dystrophy with paralysis. However, these animals did not show any skeletal lesions. It has been reported that diets high in glutamine and in cystine delay the development of skeletal lesions in rats fed aminonitriles. These reports, however, have not been verified by other authors.

Recently Selye and Bois (Selye, H., and Bois, P.: Proc. Soc. Exper. Biol. & Med. 94:133, 1957) were able to influence the severity of these lesions in rats with somatotrophic hormone and with cortisol. Selye also indicated (Rev. canad. biol. 16:1, 1957) that thyroxin given to rats could suppress these lesions. We have investigated the effects of 1-thyroxin and 3,5,3′ 1-tri-iodothyronine in rats treated with amino-acetonitrile and have found that low doses of 1-tri-iodothyronine suppressed the mild forms of aminonitrile poisoning, whereas extremely high doses of 1-thyroxin were necessary to accomplish the same result. Experiments now under way indicate that the beneficial action of 1-tri-iodothyronine on the amino-acetonitrile lesions is not limited to the skeleton but is a generalized effect on all mesodermal tissues.

SLIPPED EPIPHYSIS, LEGG-PERTHES DISEASE AND DISSECTING ANEURYSM OF THE AORTA IN HUMAN PATIENTS

From the studies of experimental lathyrism in animals, new understanding has been obtained of an epiphyseal plate lesion responsible for slipped epiphysis and Legg-Perthes disease in human patients. The epiphyseal plate lesion in these patients resembles the lesion produced in rats and rabbits with aminonitriles.

Core biopsies of the femoral neck and head have been obtained in patients with the early stages of slipping upper femoral epiphysis.[18] The joint cartilage and bone of the femoral head and neck appear to be normal on histologic examination. The epiphyseal plate is wide and greatly disrupted. The rows of proliferating cartilage cells are

disorganized, and the cells are grouped in clusters. The cartilage matrix appears to have lost its cohesion; it is fibrillated, and large clefts occur in areas of the plate with necrotic debris filling some of these clefts (Fig. 10). Occasionally blood vessels invade these disrupted areas. The endochondral ossification is interrupted in some areas but progresses well in others. Islands of cartilage cells are seen in the metaphysis. In the slides studied there were no signs of rickets, osteomalacia, osteoporosis or infection. It may be assumed that this epiphyseal lesion results in loss of strength of the plate and that it is mainly responsible for the epiphyseal slipping.

Skeletal surveys of patients with slipping upper femoral epiphysis, have shown some widening and irregularities in the outlines of other epiphyseal plates, which suggest that the lesion is not restricted to the upper femoral plate. The similarity of the epiphyseal plate lesion in human patients and in experimental animals does not, of course, imply a similar pathogenesis. It appears that the underlying cause of epiphysiolysis in human beings is probably a metabolic disturbance, but it is not known whether this disturbance is related to an inability of the organism to neutralize nitriles which may be produced in the catabolism of the proteins or whether it is related to some other metabolic aberration Chromatographic patterns of urinary amino acids, with phenol and lutidine being used as reagents, showed consistently high values for taurine, histidine and serine in children with slipping femoral epiphysis The distribution, rather than the quantity, of amino acids is altered in the urine of these patients. These findings are somewhat similar to those observed in children with adolescent scoliosis.[26]

Biopsies of the upper femoral epiphyseal plate obtained in patients with Legg-Perthes disease showed a lesion similar to that observed in patients with slipping femoral epiphysis.[16] The epiphyseal plate is wide and greatly distorted, and the endochondral ossification is irregular, proceeding normally in some areas and lacking in others. The femoral head is necrotic. It appears that in Legg-Perthes disease the faulty epiphyseal plate cartilage is the primary lesion. The necrosis of the epiphysis ensues when its blood supply becomes interrupted. We surmise that this interruption occurs when the retinacular vessels cross the thick layers of cartilage at the edge of a badly disrupted epiphyseal plate. The rent formation and some jarring of a weakened plate due to trauma may be enough to impair the continuity of these vessels before they reach the ossifying femoral head. The vessels of the ligamentum teres cannot offer any relief to the ischemic femoral head because they do not enter the bone until the ossification has extended to the fovea, usually after the 10th year of life.

Tongues formed by degenerated, eosin-stained cartilage are seen in the metaphysis and often terminate in large islands of cartilage surrounded by areas of endochondral ossification. No osteoid tissue is seen. There were no inflammatory cells in the cases studied by us. The distortion of the endochondral ossification is not caused by a defect of calcification, such as occurs in rickets, but is due presumably to disturbed maturation of the cartilage: no ossification occurs in the fibrillated areas containing large amounts of granular matrix. The roentgenograms of patients with early Legg-Perthes disease revealed a zone of decreased density in the metaphysis and an irregular epiphyseal plate.[12] These changes are explained by the distorted endochondral ossification and the large tongues and islands of cartilage in the metaphysis, as seen in the biopsy specimens.

Legg-Perthes disease is probably not localized to the upper portion of the femur. Gall and Bennett[10] in the postmortem study of one case with bilateral Legg-Perthes disease found irregularities of the upper femoral epiphyseal plate and marked derangement of the cartilage-cell columns. They also ob-

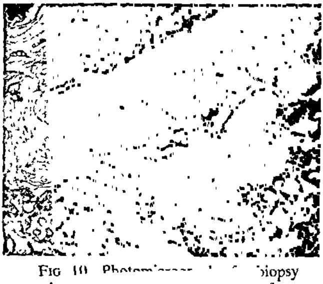


FIG 10 Photom[illegible] biopsy speci[illegible] fem- oral [illegible]-year- old girl with a slight degree of epiphyseal slipping. The epiphyseal plate is very wide, and an extensive cleft is seen extending through the middle.

onstrated deposition of S^{35} in the epiphyseal plates in about equal amounts in experimental and control animals. A high concentration of S^{35} was observed in experimental rats at the site of periosteal detachments overlying areas of new bone formations. The uptake of S^{35} by chondroitin sulfate was the same in experimental as in control animals; therefore, it may be assumed that the sulfur content of the chondroitin sulfate is not altered greatly in odoratism. These findings appear to be in accordance with the work of Bauer *et al.*[2]

It has been reported that diets high in vitamin E, in casein and in gelatin give partial protection from the lesions of lathyrism.[1,6,7] These reports have not been corroborated by other authors.[20] Neither vitamin E nor many other antioxidants tried in experimental diets have proved to be of value in delaying the development of skeletal lesions in lathyrism. A possible relationship between vitamin E and the ground substance is not well understood. Rats placed on vitamin E deficient diets for periods of 4 to 7 months developed severe testicular atrophy and muscle dystrophy with paralysis. However, these animals did not show any skeletal lesions. It has been reported that diets high in glutamine and in cystine delay the development of skeletal lesions in rats fed aminonitriles. These reports, however, have not been verified by other authors.

Recently Selye and Bois (Selye, H., and Bois, P.: Proc. Soc. Exper. Biol. & Med. 94:133, 1957) were able to influence the severity of these lesions in rats with somatotrophic hormone and with cortisol. Selye also indicated (Rev. canad. biol. 16:1, 1957) that thyroxin given to rats could suppress these lesions. We have investigated the effects of l-thyroxin and 3,5,3′ l-tri-iodothyronine in rats treated with amino-acetonitrile and have found that low doses of l-tri-iodothyronine suppressed the mild forms of aminonitrile poisoning, whereas extremely high doses of l-thyroxin were necessary to accomplish the same result. Experiments now under way indicate that the beneficial action of l-tri-iodothyronine on the amino-acetonitrile lesions is not limited to the skeleton but is a generalized effect on all mesodermal tissues.

SLIPPED EPIPHYSIS, LEGG-PERTHES DISEASE AND DISSECTING ANEURYSM OF THE AORTA IN HUMAN PATIENTS

From the studies of experimental lathyrism in animals, new understanding has been obtained of an epiphyseal plate lesion responsible for slipped epiphysis and Legg-Perthes disease in human patients. The epiphyseal plate lesion in these patients resembles the lesion produced in rats and rabbits with aminonitriles.

Core biopsies of the femoral neck and head have been obtained in patients with the early stages of slipping upper femoral epiphysis.[18] The joint cartilage and bone of the femoral head and neck appear to be normal on histologic examination The epiphyseal plate is wide and greatly disrupted. The rows of proliferating cartilage cells are

disorganized, and the cells are grouped in clusters. The cartilage matrix appears to have lost its cohesion; it is fibrillated, and large clefts occur in areas of the plate with necrotic debris filling some of these clefts (Fig. 10). Occasionally blood vessels invade these disrupted areas. The endochondral ossification is interrupted in some areas but progresses well in others. Islands of cartilage cells are seen in the metaphysis. In the slides studied there were no signs of rickets, osteomalacia, osteoporosis or infection. It may be assumed that this epiphyseal lesion results in loss of strength of the plate and that it is mainly responsible for the epiphyseal slipping.

Skeletal surveys of patients with slipping upper femoral epiphysis, have shown some widening and irregularities in the outlines of other epiphyseal plates, which suggest that the lesion is not restricted to the upper femoral plate. The similarity of the epiphyseal plate lesion in human patients and in experimental animals does not, of course, imply a similar pathogenesis. It appears that the underlying cause of epiphysiolysis in human beings is probably a metabolic disturbance, but it is not known whether this disturbance is related to an inability of the organism to neutralize nitriles which may be produced in the catabolism of the proteins or whether it is related to some other metabolic aberration. Chromatographic patterns of urinary amino acids, with phenol and lutidine being used as reagents, showed consistently high values for taurine, histidine and serine in children with slipping femoral epiphysis The distribution, rather than the quantity, of amino acids is altered in the urine of these patients. These findings are somewhat similar to those observed in children with adolescent scoliosis.[20]

Biopsies of the upper femoral epiphyseal plate obtained in patients with Legg-Perthes disease showed a lesion similar to that observed in patients with slipping femoral epiphysis.[16] The epiphyseal plate is wide and greatly distorted, and the endochondral ossification is irregular, proceeding normally in some areas and lacking in others. The femoral head is necrotic. It appears that in Legg-Perthes disease the faulty epiphyseal plate cartilage is the primary lesion. The necrosis of the epiphysis ensues when its blood supply becomes interrupted. We surmise that this interruption occurs when the retinacular vessels cross the thick layers of cartilage at the edge of a badly disrupted epiphyseal plate. The rent formation and some jarring of a weakened plate due to trauma may be enough to impair the continuity of these vessels before they reach the ossifying femoral head. The vessels of the ligamentum teres cannot offer any relief to the ischemic femoral head because they do not enter the bone until the ossification has extended to the fovea, usually after the 10th year of life.

Tongues formed by degenerated, eosin-stained cartilage are seen in the metaphysis and often terminate in large islands of cartilage surrounded by areas of endochondral ossification. No osteoid tissue is seen. There were no inflammatory cells in the cases studied by us. The distortion of the endochondral ossification is not caused by a defect of calcification, such as occurs in rickets, but is due presumably to disturbed maturation of the cartilage: no ossification occurs in the fibrillated areas containing large amounts of granular matrix. The roentgenograms of patients with early Legg-Perthes disease revealed a zone of decreased density in the metaphysis and an irregular epiphyseal plate.[12] These changes are explained by the distorted endochondral ossification and the large tongues and islands of cartilage in the metaphysis, as seen in the biopsy specimens.

Legg-Perthes disease is probably not localized to the upper portion of the femur. Gall and Bennett[10] in the postmortem study of one case with bilateral Legg-Perthes disease found irregularities of the upper femoral epiphyseal plate and marked derangement of the cartilage-cell columns. They also ob-



FIG. 11. Photomicrograph of the epiphyseal plate of the 1st thoracic vertebra of a 160-day-old rat fed a stock diet containing 50 per cent *Lathyrus odoratus* seeds from 60 days of age. The cartilaginous plate is ossified. The epiphyseal plate is very wide and greatly distorted. The annulus fibrosus is seen at the upper part of the picture.

served similar irregularities in the epiphyseal plate of the greater trochanter, of the acetabulum and of the costochondral junctions. Apparently other epiphyseal plates were not examined. Often skeletal surveys of patients with Legg-Perthes disease show some irregularity in other epiphyseal plates. The peculiar blood supply of the femoral head probably accounts for the more serious consequence of the lesions of the upper femoral epiphyseal plate than in any other epiphysis.

No records are available in the literature of histologic studies of the vertebrae of patients with scoliosis during the progressive stages of the deformity. A number of observations, however, point to a defect in the epiphyseal plates of the vertebrae. It is well known, for example, that "idiopathic" scoliosis occurs in adolescents, and the deformity ceases to progress as soon as the skeletal growth of the spine is completed; that is, as soon as the epiphyseal plates become obliterated Dr. Farkas[9] has studied the roentgenographic changes of the spine in patients with "idiopathic" scoliosis and has pointed to defects of the vertebrae in areas adjacent to the cartilaginous plate It should be noted that diseases in children which produce widening and weakening of the epiphyseal plates such as rickets or even vitamin D resistant rickets, do not cause scoliosis. It appears that weakening of the epiphyseal plates alone will not produce scoliosis unless it is accompanied by weak-

ening of the ligamentous insertions into the vertebrae and ribs that help to stabilize the spine.

The pathogenesis of adolescent kyphosis can be explained on the basis of defects of the epiphyseal plates of the vertebrae similar to the lesions described in the experimental animals fed aminonitriles (Fig. 11). Scheuermann,[22] basing his studies on clinical and roentgenographic data, proposed a similar pathogenesis. Schmorl's theory, which maintains that prolapse of the nucleous pulposus is the primary factor in adolescent kyphosis, does not explain the fact that the kyphosis stops progressing as soon as the skeletal growth of the spine is completed. The defects of ossification present in the metaphysis of the involved vertebrae may represent fibrous tissue defects.

The occurrence of dissecting aneurysm of the aorta in human patients with kyphoscoliosis has been studied recently.[3] Of 20 patients who died of dissecting aneurysm of the thoracic aorta, 7, or 35 per cent, had gross skeletal abnormalities; 5 had deforming kyphoscoliosis; and 2 had severe pigeon-breast deformity. Often patients with Marfan's syndrome also die of dissecting aneurysm of the aorta.

The suppression with 1-tri-iodothyronine of the epiphyseal plate lesions and scoliosis in rats fed aminonitriles suggests a possible beneficial effect of 1-tri-iodothyronine in human beings with similar skeletal disorders. A clinical trial with this drug may be justified

REFERENCES

1 Bachhuber, T E., Lalich, J. J , Angevine, D. M., Schilling, E. D., and Strong, F. M. Lathyrus factor activity of aminopropionitrile and related compounds, Proc Soc. Exper. Biol. & Med 89:294-297, 1955.

2. Bauer, G., Carlsson, A., and Lindquist, B : Skeletal uptake of sulfate and phosphate in aminopropionitrile poisoned rats, Acta path. et microbiol scandinav. 37:617, 1954.

3. Bean, William, B , and Ponseti, I. V.: Dissecting aneurysm produced by diet, Circulation 12:185, 1955

4. Chang, C. Y., Witschi, E., and Ponseti, I. V.: Teratogenic effects of *Lathyrus odoratus* seeds on development and regeneration of vertebrate limbs, Proc. Soc. Exper. Biol. & Med. 90:45-60, 1955.

5. Dasler, Waldemar: Isolation of toxic crystals from sweet peas *(Lathyrus odoratus)*, Science 120:307-308, 1954.

6. ———: Partial protection against odoratism (sweet pea lathyrism) by diets high in gelatin or casein, Proc. Soc. Exper. Biol. & Med. 85:485-488, 1954.

7. ———: Protective action of glutamine, cysteine and other substances against experimental lathyrism in the rat, Proc. Soc. Exper. Biol. & Med. 91:554-557, 1956.

8 Dupuy, H. P., and Lee, J. G.: Isolation of a material capable of producing experimental lathyrism, J. Am. Pharm. A. 43: 61-62, 1954.

9. Farcas, Aladar: The pathogenesis of idiopathic scoliosis, J. Bone & Joint Surg. 36A: 617, 1954.

10 Gall, E. A., and Bennett, G. A.: Osteochondritis deformans of the hip (Legg-Perthes disease) and renal osteitis fibrosa cystica; report of a case with anatomic studies, Arch. Path. 33:866-878, 1942.

11. Geiger, B. J., Steenbock, Harry, and Parsons, H. T.: Lathyrism in the rat, J. Nutrition 6:427-442, 1933.

12 Gill, A. B.: Legg-Perthes disease of the hip; its early roentgenographic manifestations and its clinical course, J. Bone & Joint Surg. 22:1013-1047, 1940.

13. Jiménez Diaz, C., and Vivanco, F.: Investigaciones sobre el cicerismo, Rev. méd. españ. 33:393, 1949.

14. Lewis, H B., Fajans, R. S., Esterer, M. B., Shen, C. W., and Oliphant, M.: The nutritive value of some legumes: Lathyrism in the rat, the sweet pea *(Lathyrus odoratus)*, *Lathyrus sativus*, *Lathyrus cicera* and some other species of Lathyrus, J. Nutrition 36: 537-559, 1948.

15 Lewis, H. B., and Schulert, A. R.: Experimental lathyrism in the white rat and mouse, Proc. Soc. Exper. Biol. & Med. 71: 440-441, 1949.

16 Ponseti, I. V. Legg-Perthes disease, J. Bone & Joint Surg 38A:739-750, 1956.

17. Ponseti, I. V., and Baird, W. A.: Scoliosis and dissecting aneurysm of the aorta in rats fed with *Lathyrus odoratus* seeds, Am. J. Path. 28:1059-1077, 1952.

18. Ponseti, I. V., and McClintock, R.: The pathology of slipping of the upper femoral

epiphysis, J. Bone & Joint Surg. 38A:71-83, 1956.
19. Ponseti, I. V., and Shepard, R. S.: Lesions of the skeleton and other mesodermal tissues in rats fed sweet-pea *(Lathyrus odoratus)* seeds, J. Bone & Joint Surg 36A:1031-1058, 1954.
20. Ponseti, I. V., Wawzonek, S., Shepard, R. S., Evans, T. C., and Stearns, G.: Further studies on lathyrism in the rat, Proc. Soc. Exper. Biol. & Med. 92:366-369, 1956.
21. Puig, J. Simarro, and deViñals, R. Roca: Aportación a la anatomía patológica del latirismo, Rev. clín. españ. 8:107, 1943.
22. Scheuermann, H.: Roentgenologic studies of the origin and development of juvenile kyphosis, together with some investigations concerning the vertebral epiphyses in man and in animals, Acta orthop. scandinav. 5: 161-220, 1934.
23 Schilling, E. D., and Strong, F. M.: Isolation, structure and synthesis of a Lathyrus factor from *L. odoratus,* J. Am. Chem. Soc. 76:2848, 1954.
24. Schuchart, Von Bernh: Zur Geschichte und Casuistik des Lathyrismus, Deutsches Arch. klin. Med. 40:312-341, 1887.
25. Stamler, F. W.: Reproduction in rats fed Lathyrus peas or aminonitriles, Proc. Soc. Exper. Biol. & Med. 90:294-298, 1955.
26. Stearns, G., Chen, Jo-Yun Tung, McKinley, J. B., and Ponseti, I. V.: Metabolic studies of children with idiopathic scoliosis, J. Bone & Joint Surg. 37A:1028-1034, 1955.
27. Stockman, R.: Lathyrism, J. Pharmacol & Exper. Therap. 37:43-53, 1929.
28. Strong, F. M.: Lathyrism and odoratism, Nutrition Rev. 14:65, 1956
29. Vivanco, F., and Jiménez Diaz, C.: Nuevos estudios sobre los efectos de las proteinas de las legumbres (leguminismos), Rev. clín. españ. 40:157-162, 1951.
30. Wawzonek, S., Ponseti, I. V., Shepard, R. S., and Wiedenmann, I. G.: Epiphyseal plate lesions, degenerative arthritis, and dissecting aneurysm of the aorta produced by aminonitriles, Science 121:63-65, 1955.

Lesiones Skeletic Producite per Aminonitriles

Summario in Interlingua

Le uso alimentari de certe pisos del genere *Lathyrus* produce in vertebratos un debilitation del placas epiphysal de ossos longee un relaxation del insertiones ligamentose. Ha essite determinate que le composito active que es responsabile pro iste lesiones es beta-aminopropionitril (BAPN). Aminoacetonitril (AAN) e methyleneaminoacetonitril addite al dieta del vertebratos es plus active que BAPN in le production del lesiones skeletic.

Le lesion del placa epiphysal in animales experimental es characterisate per un allargamento del placa epiphysal in consequentia de un augmento del cellulas cartilaginose. Iste cellulas es arrangiate sin ordine. Le matrice cartilaginose pare perder su cohesion. Fissuras occurre in le placa epiphysal, e dislocationes epiphysal pote evenir. Le aminonitriles etiam causa un perdita de cohesion del matrice cartilaginose al sito del insertiones ligamentose, e iste insertiones deveni relaxate e partialmente distachate ab le osso subjacente. Il occurre un abundante neoformation de periosteo Le cyphoscoliosis que se disveloppa in animales experimental es le effecto de un dislocation vertebral al sito del placa epiphysal. Osteoarthritis occurre in multe articulationes, e in juvene rattos le disveloppamento de aneurysma dissecante pote effectuar se.

Biopsias a puncion in patientes human qui suffre de dislocation del epiphyse superofemoral e de morbo de Legg-Perthes ha demonstrate in le placa epiphysal le presentia de un lesion simile a illo producite per aminonitriles in animales experimental. Ha etiam essite constatate que le osteoarthritis e le aneurysma dissecante del aorta que se incontra in patientes human es histologicamente simile al lesiones producite in rattos per le administration de aminonitriles.

Section II

GENERAL ORTHOPAEDICS

12

Periosteal Myxoma of Infancy and Periosteal Chondroma of Adolescence, with Local Malignancy*

O. SCAGLIETTI, M.D., AND G. STRINGA, M.D.†

The two types of primitive bone tumors described here are rarely encountered in clinical practice. In over 2,000 cases of bone tumors seen at the Tumor Center of Florence, only six similar lesions were found. They deserve mention here not only because of their rarity but also because of the relationships that seem to exist between the two forms. Actually there are two varieties: the two types differ in their age of development, site, evolution and histology. However, after an accurate study which takes their histogenesis, their general clinical aspects and their final prognosis into account, one can conclude that actually there are such points of contact between these two varieties that one can approach them under a single heading.

We will describe the two neoplasms separately in order to be able to find the analogies afterward.

METAPHYSEAL MYXOMA OF INFANCY

NOTES FROM THE LITERATURE

This neoplasm is little known in the literature. Geschickter and Copeland (1949) and Hellner (1950) do not even mention it in their textbooks; Coley (1949) gives only a few lines to myxoma of the bone; Herzog (1944) reports the histologic and the pathologic aspects but not the clinical or the roentgenologic aspects.

A brief description of a case is given by Bauer and Harrel (1954); Jaffe and Lichtenstein (1948) describe a few cases under the name "chondromyxoid fibroma of the bone" which have a histologic aspect that substantially is similar to ours (myxomatous) and a radiologic aspect which approaches our case. On the other hand, the age of development reported by those authors is far older than ours (in all cases the age was over 13: 17, 18, 22, 28, etc.); one can easily find cartilaginous aspects near myxomatous ones (which is not so in our cases); the clinical course is slower and absolutely benign, without relapses even after incomplete curettage (our cases had local malignancy).

CLINICAL CHARACTERISTICS

The age of myxomas is strictly limited: all three cases observed were from 5 to 6 years old. The lesion develops rather rapidly; the symptomatology developed from 20 to 40 days earlier. The symptoms consist of pain and limping, tumefaction of a fibrous cartilaginous consistency coming from the skeleton and pain on local pressure. In the space of a few weeks from the beginning of symptoms, the extremity already is deformed because of the tumefaction.

* Translated from the Italian by Medical Literature Service, 19 South 22nd Street, Philadelphia 3, Pa

† Florence, Italy



FIGS. 1-9, Case 1. Periosteal myxoma of infancy. Boy 6 years of age.

FIG. 1 *(above)*. Pain and swelling of the lower third of the leg. Clearing of the inferior metaphysis of the tibia with distinct margins and notable periosteal reaction.

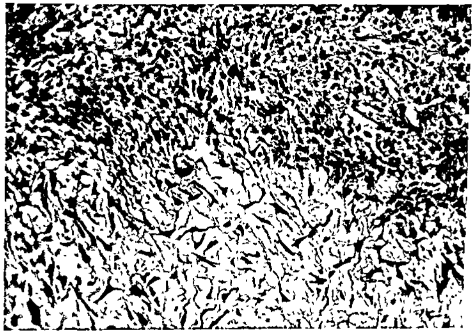


FIG. 2. Biopsy during curettage: myxomatous tissue with more richly cellular and proliferative areas.



FIG. 3. Fourteen months after curettage: local relapse in the form of a polycystic cavity.

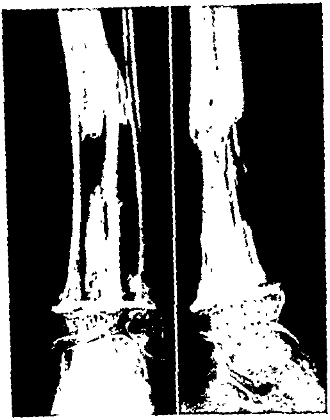


FIG. 4. A month after complete resection of the metaphysis and its substitution by bone segments taken from the contralateral tibia.

ROENTGENOLOGIC CHARACTERISTICS

This is a radiotransparent lesion of subperiosteal extracortical origin, located in the metaphysis. The sites encountered by us are the superior femoral metaphysis, the superior tibial metaphysis and the inferior tibial metaphysis. The tumor appears as a round transparent area, located in the spongiosa of the metaphysis, which extends partially outside the boundaries of the bone and is partially retained and confined by the notable periosteal reaction (Figs. 1 & 11-13). The radiotransparent area is of great dimensions, adherent to or a short distance from the cartilage of conjugation, with neat margins in the surrounding spongy tissue. An imposing, highly condensing, periosteal reaction, sometimes accompanied by stratified deposition parallel to the bone, confines the tumor, assuming in profile the aspect of a triangular sharp spur.

One reaches the roentgenologic state described above very rapidly, in the space of a few weeks, if one considers the brief period of time since the beginning of the clinical symptoms.

The aspect of the relapses is interesting (in fact, all three cases were treated with curettage, and all three relapsed—Figs. 3, 10 [right] & 12).

The roentgenologic characteristics of the relapses are absolutely the same in all three cases; instead of the single radiotranslucent area of the initial stage, the neoplasm is represented by an agglomeration of almost round areas of unequal dimensions, so that they give the appearance of a polycystic lesion of the metaphysis.

In differential diagnosis the essential osseous cyst should be considered above all in its acute giant-cell variety.

ANATOMOPATHOLOGIC CHARACTERISTICS

Upon microscopic examination the neoplasm appears to be well contained by the still uninvolved periosteum (Figs. 6 & 7); the tumor evidently has its beginning be-



FIG. 5. Six years after resection: no sign of local relapse, no shortening and good function of the tibiotarsal joint.

tween the cortex and the periosteum, pushing the periosteum in front of itself in the process of growing and slowly eroding the cortex. Since the cortex is thin at the metaphysis, while the periosteum is more robust, being reinforced by ligamentous and capsular expansions, the neoplasm is contained by the periosteum while it expands into the spongiosa Here the healthy tissue forms a stratum of bone that contains the tumor which, in the final analysis, remains above the site of the cortex, partially progressing toward the bone tissue and partially extending toward the outside. As a result, in the relapsed form the specimen is composed of an agglomeration of intercommunicating cavities filled with mucilaginous fluid.

The tumor tissue has either a myxoid cartilaginous appearance, with the usual white luminous color of mother-of-pearl, or a lower consistency with almost fluid areas of a myxomatous type.

The prevailing component of this neoplasm is a myxomatous tissue with some in-



FIG. 6. Showing the anatomic section immediately after resection

dication of malignancy (Fig. 8), composed of stellate or fusiform cells, cut off and scattered in an abundance of basic substance. The nucleus is polymorphic, kidney shaped or elongated; the cytoplasm is abundant and provided with prolongations that mix with similar prolongations from other cells. The cells are arranged in lobules: at the periphery we find fused cells, elongated and densely packed together, which represent the proliferative layer by which the tumor grows.



FIG. 7. The histologic section of the entire fragment.

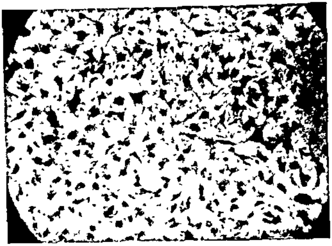


FIG. 8. A histologic aspect: myxomatous tissue, stained with hematoxylin-eosin.

There is no clear capsule round each lobule, nor does one enclose the neoplasm; therefore, although arranged within a lobular architecture, it possesses aggressive and infiltrating abilities at the periphery of each lobule.

The reactions to dyes are typical of myxomatous tissue; in fact, the sections are stained metachromatically with Toluidine Blue, Victoria Blue, etc., and are stained intensely with the basic dyes.

The interlobular stroma is furnished by the tissue of the host, that is, by the bone marrow. The presence in the stroma of numerous giant cells with 6 to 15 nuclei in direct contact with the peripheral layer of the lobule is characteristic, probably expressing an attempt at defense on the part of the bone marrow against the foreign body represented by the neoplasm.

The fragments extracted with the first curettage always made possible an exact diagnosis with the prediction of a relapse due to the mildly malignant characteristics (Fig. 2).

Prognosis and Treatment

The clinical course was fairly rapid; the roentgenogram showed progressive invasion of the osseous structures; the histologic findings showed many malignant changes; the local relapse after inadequate therapy justifies calling it a neoplasm with aggressive tendencies, or a local malignancy. The treatment of choice is thus total resection of the involved segment. In fact, our cases, which were all operated upon for the first time with simple curettage, presented all the signs of relapse in a variable period of 3 to 8 months.

Because of the relapse, resection was carried out, followed by transplantation of autoplastic bone from the other tibia to substitute for the extirpated segment. The cases were reviewed four to thirteen years later without finding any local symptoms; they were in optimal general condition, with functioning extremities (Figs. 4 & 5).

PERIOSTEAL CHONDROMA OF ADOLESCENCE

Notes from the Literature

This type, located at the diaphysis, is better known than the one mentioned previously, and its description may be encountered more frequently in books and monographs concerning the cartilaginous tumors



FIG. 9. The boundary between the tumoral tissue (toward the bottom of the figure, bounded by a more richly cellular and proliferative area) and the normal bony structure of the metaphysis, in the process of osteoclastic reabsorption (here one can see giant cells enclosed in the wall of the bone).

of the bones. A similar roentgenogram is reported, for example, on page 124 of the textbook of Geschickter and Copeland under the title "Degenerated Exostosis."

CLINICAL CHARACTERISTICS

The three subjects of the present cases were from 12 to 13 years old. The first symptoms appear four to five months ahead: tumefaction or slight pain, with a slower evolution than in the form described previously.

ROENTGENOLOGIC CHARACTERISTICS

The lesion is located on the diaphysis; in two cases it was at the boundary of the diaphysis and the *metaphysis* (Figs. 14 & 15); in the third case it was completely in the diaphysis. The neoplasm has an extracortical location, putting it almost completely outside the normal boundaries of the bone *In an advanced stage the lesion is* represented as a radiotranslucent mass which is almost completely outside the bone and is circumscribed, as though encased, by a severe periosteal reaction which forms a triangular spur proximally and distally, bounding the neoplasm all round. In the *cortex, a niche is excavated through which* the neoplasm may reach the medullary channel. In differential diagnosis, an inflammatory periostitic process may be discussed at first. In a more advanced stage, there are no doubts about the fact that the lesion is *tumoral, cartilaginous and not at all benign.*

ANATOMOPATHOLOGIC CHARACTERISTICS

The neoplasm is subperiosteal, like the *metaphyseal one described previously,* but it develops differently due to the different anatomic conditions in the diaphysis, as compared with the metaphysis: *the robust* cortex yields only slowly to the osteoclastic reabsorption, while the periosteum is pushed out more rapidly (Fig. 16). The reaction of *the periosteum is impressive here,* it being pushed out of the cortex in such a way that one would say that it accompanies the growth of the lesion, following the peripheral level; the cortex, reinforced by the *periosteal proliferation, constitutes a crater with* raised borders in whose fossa the tumor is included. The tumor tissue is cartilaginous, with a white, mother-of-pearl color.

In time, the pressure of the tumor succeeds in perforating the cortex, and the tumor expands into the medullary channel: *in an advanced process it arrives at a knap*sack shape with the major portion being

extracortical, the minor portion intramedullary.

The prevailing tissue is composed of cartilage, united in lobules, while in the periphery, that is, in the area of growth, there are myxomatous areas and precartilaginous embryolike connective tissues.

In the lobule the structure is typically cartilaginous, the cells sometimes being in mucous degeneration and capsulated. Areas with calcareous precipitation and large necrotic zones are found inside the body of the tumor. They are seen in contact with the periosteal reaction areas of metaplastic ossification.

The peripheral areas are composed of cells which are more compact, elongated, fusiform and young.

PROGNOSIS AND TREATMENT

Even with this neoplasm, as with the one previously described, one could speak of a neoplasm with local malignancy, considering the rapid course, the osseous invasion, the notable radiating periosteal reaction and the relapse in cases of incomplete treatment. It is advisable, therefore, to resect the bony segment of the neoplasm, substituting for it bony segments obtained from the contralateral tibia. In our cases we carried out resection and successive osseous transplantation. In one case a simple curettage was done, followed in the space of three months by a local relapse. All the cases seen again 4-6-9 years later presented reconstitution of the skeletal segment with normal or almost normal function.

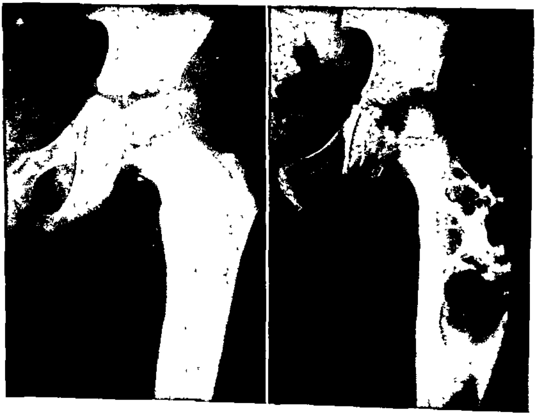
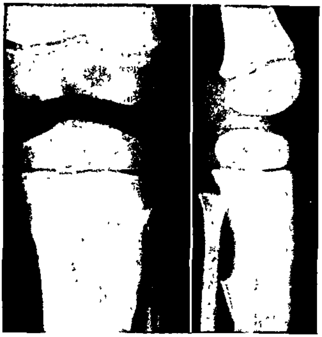


FIG. 10, Case 2. Periosteal myxoma of infancy. Boy 5 years of age. The child had pain in the root of the leg and limbs for 40 days. *(Left)* Shows a round area of rarefaction in the superior femoral metaphysis. Simple curettage was done but was followed by relapse. *(Right)* In 5 months resection of the entire superior femoral extremity was performed, and after a year a fibular transplant also was done. An examination 10 years later shows no signs of local relapse, and the function of the extremity is sufficient.



FIGS. 11-13, Case 3. Periosteal myxoma. *Boy 5 years of age.*

FIG. 11 *(above)*. The child had claudication and pain for 1 month. Roentgenogram shows a rarefaction of the metaphysis, oval in shape, bounded inferiorly by a notable periosteal reaction. The curettage performed the first time was followed by local relapse after 4 months.

ANALOGIES AND THE POSSIBLE UNIFICATION OF THE TWO VARIETIES (METAPHYSEAL AND DIAPHYSEAL)

There are analogies and relationships between the two varieties, myxoma of infancy and chondroma of adolescence, with regard to the site of origin, histogenesis, roentgenogram, histology and age of development.

The origin is subperiosteal in both varieties, and the penetration toward the medullary channel is secondary. The question of origin thus is related to that of the tumors with a precartilaginous matrix and a subperiosteal location. It is difficult to say whether the points of origin are nests of embryonal precartilaginous tissue which have remained quiescent for a long time between the periosteum and the cortex or whether it is a case of sudden proliferative deviation of the periosteal strata under the impact of different stimuli.

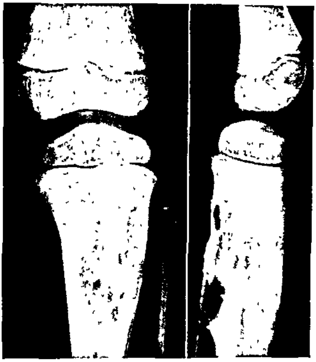


FIG. 12. An amputation was performed (Today the amputation must be considered an excessive procedure for these types of neoplasms.)

The diversity of the *x-ray characteristics* in the two forms may be attributed to the site (metaphyseal or diaphyseal), due to the different modes of reaction of the healthy tissues of the host: cortex, periosteum and spongiosa.

In the diaphysis, the neoplasm extends predominantly toward the outside, pushing the periosteum aside and only slowly perforating the cortex, which is fairly robust. In the metaphysis, the periosteum, which is more robust than the cortex, relatively con-



FIG. 13. Transverse section of the neoplasm as it appears in the histologic examination. The subperiosteal, extracortical *location* of the lesion and its lobular constitution are evident.



FIGS 14-16, Case 4. Periosteal chondroma of adolescence. Boy 12 years of age.

FIG. 14 *(above)*. The boy had had pain and tumefaction in the leg for 2 months.

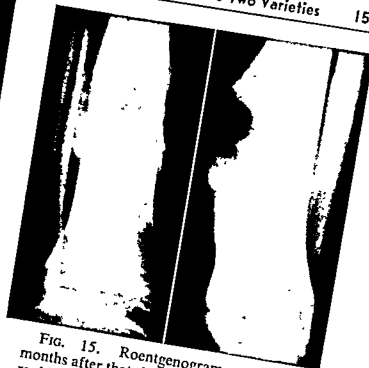


FIG. 15. Roentgenogram taken 4 months after that shown in Figure 14. The rapid progression of the lesion is evident. The curettage performed between the taking of these two roentgenograms did not have any effect. A complete resection of the metaphysis then was performed, leaving the cartilage of conjugation in place and transplanting more bony segments from the contralateral tibia. An examination performed 9 years later revealed good function of the extremity without any sign of local relapse.

tains the tumor, forcing it to erode the thin cortex and the underlying spongiosa.

From a *histologic* viewpoint, the metaphyseal variety of infancy is composed of myxomatous tissue, while the diaphyseal variety of adolescence is composed of cartilaginous tissue. In the second variety, however, it is easy to find very large peripheral areas of myxomatous tissue near the cartilaginous zones.

For the metaphyseal myxomas with rapid development, the age is 6 years; for the diaphyseal chondromas with rather slower development, it is 12 years. Because of this, and because of the preceding relationships, it is possible to maintain the hypothesis that the same lesion, if started precociously at 6 years of age, would have a metaphyseal site, myxomatous constitution and tumultuous course. If, instead, it starts later, toward 12 years of age, it will grow away from the "cartilage of conjugation," according to the known laws of osseous growth, and, by assuming a diaphyseal site, it may modify the anatomopathologic characteristics slightly, adapting them to the different local architecture and simultaneously assuming a greater histologic maturity and slower rate of development.

The tumors described by Jaffe and Lichtenstein (1948) are certainly related to these varieties, enlarging even more the concept already expressed. One can maintain that the form described by these authors, which, as is known, is developed in youth and even in advanced maturity, has a slow clinical course and histologic areas of chondroma-



FIG 16. Histologic section of the entire fragment. The neoplasm, of triangular shape, bounded superiorly and inferiorly by the periosteal resection, has perforated the cortex and penetrated into the medullary channel.

tous tumors near myxomatous ones, and does not relapse, could even be included in the same type of neoplasia already described here; however, since it starts later in life, it loses the tumultuous and aggressive characteristics of development. In fact, the development of our cases takes place within a few weeks; that of Jaffe and Lichtenstein, many months. The histologic aspect is myxomatous in the metaphyseal cases, chondromatous and myxomatous in the later diaphyseal cases, and chondromatous in those of even later date. The prognosis is that of local malignancy with easy relapses in the cases of infancy, but altogether benign in the later cases of Jaffe and Lichtenstein.

CONCLUSION

Two primitive neoplasms of the bone have been considered.

The first type of tumor, of which we have limited and fragmentary knowledge, even in the recent literature, starts at 5 to 6 years of age, is located in the metaphysis and is subperiosteal; the roentgenogram shows an oval, eccentric, bright spot in the spongiosa of the metaphysis, bounded by a periosteal reaction. The development is fairly rapid, and the histology shows myxomatous tissue with certain atypical data. It relapses after simple curettage, but it is cured permanently after resection.

The second type of tumor, encountered less rarely in the literature, develops in boys of 12 to 13 years of age. It is located in the diaphysis and is subperiosteal. The tumor develops in a few months, likewise relapsing if treated by curettage alone It is composed of cartilaginous tissue with peripheral areas of immature tissue.

The location (subperiosteal), the type of tissue (myxomatous with rare chondroid aspects in the first type, cartilaginous with immature areas in the periphery in the second type), the clinical behavior (rapid evolution, relapse), and the age of respective development (5 to 12 years) may sustain the hypothesis that it is a case of the same lesion modified in some aspects according to the age and the location of development. In summary, we are concerned here with myxocartilaginous neoplasms with discrete histologic immaturity and an extracortical origin that are subperiosteal and located either in the metaphysis or in the diaphysis, occurring in young subjects 5 to 12 years of age, with rapid development, and local relapses if treated incompletely, complete recovery if resected.

It is known from the literature that similar lesions may develop even later in life, ultimately modifying their characteristics.

SUMMARY

On the basis of 6 observed cases, two types of primitive neoplasms of the bones are described which are little known in the literature: a metaphyseal variety of early

infancy with a myxomatous constitution and a rapid development, and a diaphyseal variety of later age with a prevalently cartilaginous constitution. Analogies are discussed with regard to the histogenesis, location, clinical course and prognosis (the lesions occur with local malignancy, with relapses if treated by simple curettage), by which we could sustain the hypothesis that it is a case here of the same neoplasm developed at different periods of life.

BIBLIOGRAPHY

Bauer, W. H., and Harell, A.: Myxoma of bone, J. Bone & Joint Surg. 36A:263-266, 1954.

Bloodgood, J. C.: Myxoma, central and periosteal, Ann. Surg. 72:712-724, 1920.

Coley, B. L.: Neoplasms of Bone, New York, Hoeber, 1949.

Geschickter, C., and Copeland, M.: Tumors of Bone, Philadelphia, Lippincott, 1949.

Hellner, H.: Die Knochengeschwulste, Berlin, Springer, 1950.

Herzog, G.: Die primaeren Knochengeschwulste *in* Handbuch der spez. Path. Anat. u. Hist., vol. 9, chap. 5, Berlin, Springer, 1944.

Jaffe, H. L., and Lichtenstein, L.: Chondromyxoid fibroma of bone, Arch. Path. 45:541-551, 1948.

Stout, A. P.: Myxoma, the tumor of primitive mesenchyme, Ann. Surg. 127:706-719, 1940.

Myxoma Periosteal de Juveniles e Chondroma Periosteal de Adolescentes, de Malignitate Local

Summario in Interlingua

Es discutite duo neoplasias primitive del osso.

Le prime de iste typos de tumor esseva, usque recentemente, representate in le litteratura per solmente limitate e fragmentari reportos. Illo se declara al etate de 5 a 6 annos Su sito es metaphysari, subperiosteal Le aspecto radiographic es un eccentric transparentia ovalesc in le spongiosa metaphysari, delimitate per densitates periosteal. Le disveloppamento del tumor es satis rapide. Le histologia es myxomatose con certe characteristicas atypic. Simple curettage es sequite de recidiva. Resection resulta in curation permanente.

Le secunde typo de tumor se trova minus rarmente in le litteratura. Illo se disveloppa in adolescentes de 12 a 13 annos. Su sito es diaphysari, subperiosteal. Le tumor se evolve in le curso de alicun menses. In su caso, simple curettage resulta equalmente in recidiva Illo es componite de histos cartilaginose con un area peripheric de histos immatur.

Le identitate del sito (subperiosteal); le typo de histo (myxomatose con rar aspectos chondroide in le prime typo e cartilaginose con areas immatur peripheric in le secunde typo); le comportamento clinic (evolution rapide con recidivas post curettage); e le etate del declaration in le due casos (5 annos a 12 annos) servi a supportar le hypothese que il se tracta de un sol lesion con modification de certe aspectos secundo le etate e le sito de su disveloppamento. Il se tracta in summa de neoformationes myxocartilaginose con discrete immaturitate histologic, origine extracortical, subperiosteal, e sito meta- o diaphysari, que occurre in juvene subjectos de 5 a 12 annos, que ha un disveloppamento rapide, e que responde per recidivas local si illo es tractate incompletemente sed per un curation complete si illo es resecate. Le litteratura indica que lesiones analoge pote disveloppar se ancora plus tarde in le vita. Alora le characteristicas es additionalmente modificate.

13

Abnormal Ribs in the Cervical Region Associated with Sprengel's Deformity

G. I. W. COTTAM, M.D., F.A.C.S.,
AND ROBERT E. VANDEMARK, M.D., F.A.C.S.*

Developmental failure of the scapula to descend completely to its normal adult position has long been known as Sprengel's deformity. Associated with scapular deformity, frequently there are connections between the scapula and the spine which may be osseous ("omovertebral bone"), cartilaginous or ligamentous. Cervical ribs may be present in as many as 31.4 per cent of the cases and other rib abnormalities in 48.5 per cent of cases.[4] Various operative procedures[2,3,5,6,7] have been described for "undescended scapula," but, undoubtedly, that of Schrock[5,6] has been recognized most generally. Surgery is neither necessary nor desirable in every case of Sprengel's deformity; the operative indications are marked deformity, pain and limitation of motion. These have been emphasized recently by Greville and Coventry.[3]

It is to those cases, where operation is indicated and abnormal cervical ribs are present, that our attention is focused in this discussion.

The pressure produced by cervical ribs on adjacent nerves and vessels is well known. The postoperative complication of brachial paralysis in Sprengel's deformity has long been recognized. As recently as 1952 a report of this postoperative complication in 12.5 per cent of cases of Sprengel's deformity was made. In these cases various operative procedures were used to move the scapula and the shoulder caudally. No discussion of the problem of postoperative paralysis was made, except to state that attempts at overcorrection should be condemned. In 4 cases, the same author reported that no attempt was made to correct the abnormal position of the scapula. In these 4 cases surgery was restricted to bony resection of the superomedial portion of the

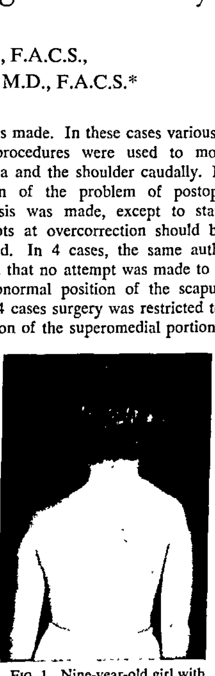


FIG. 1. Nine-year-old girl with congenital elevation of the scapula, the right acromion being about 2 inches higher than the left.

* Sioux Falls, South Dakota.



FIG. 2. Roentgenogram showing, in addition to the elevated scapula, abnormally curved and high right 1st and 2nd ribs, fusion of 4th, 5th and 6th right ribs and an upper dorsal scoliosis.

scapula and excision of an omovertebral bone in 3 cases. Abduction was increased in 2 of 3 patients in whom it had been restricted before operation.

It was the opinion of one of us (R.E.V.) that the abnormal ribs in the cervical area might well be one of several factors contributing to the postoperative paralysis following transplantation of the scapula, and excision of the abnormal rib or ribs, as a preliminary procedure, was worthy of consideration. Accordingly, in 1953, it was elected to excise the abnormal ribs through a posterior incision, which later was used for transplantation of the scapula. The case is reported as follows:

CASE REPORT

The patient, a white female child of 9 years, was born with a marked deformity of the right shoulder. At the age of 5 months, a diagnosis of Sprengel's deformity had been made. Clinical examination showed a rather severe deformity of the right shoulder, the right acromion being about 2 inches (5.08 cm.) higher than the left (Fig. 1). There were visible and palpable prominences in the right supraclavicular area, and a roentgenogram (Fig. 2) showed abnormally high, curved, right first and second ribs. In addition to the elevated scapula, the fouth, fifth and sixth right ribs were fused, and a right upper dorsal scoliosis was present. No attempt had been made to correct the deformity.

It was felt that local resection of the superomedial scapula would only bring the high cervical ribs into further prominence and would not lower the acromial level (Fig. 1). In reviewing the roentgenograms (Fig. 2), it was evident that a considerable length of the brachial plexus and [illegible] length and mobility to move the scapula downward. Accordingly, it was elected to perform a preliminary cervical rib resection, to be followed by transplantation of the scapula.

The patient was admitted to the hospital on July 16, 1953, and the ribs were operated on the following day (by G.I.W.C.) under ether-nitrous oxide-oxygen anesthesia, following an induction with intravenous Pentothal Sodium.[1] Through a posterior incision, portions of the first and the second right ribs were resected subperiosteally. The operation was interrupted by a generalized convulsion and a high rectal temperature of 40° C. (104° F.). While the cause was unknown, it was speculated that it might be an ether convulsion. The wound was closed as rapidly as possible, and a small rent was torn in the pleura to cause some pneumothorax, which was treated in the usual manner. Roentgenograms showed the ribs to have been well excised; the patient's postoperative course was good. She left the hospital on July 29, to return for the scapular transplantation within the next few weeks.

On January 5, 1954, the patient was next seen. Roentgenograms at this time showed the ribs to be reforming to such an extent that re-excision was advisable; this was done on May 28, 1954.

13

Abnormal Ribs in the Cervical Region Associated with Sprengel's Deformity

G. I. W. COTTAM, M.D., F.A.C.S.,
AND ROBERT E. VANDEMARK, M.D., F.A.C.S.*

Developmental failure of the scapula to descend completely to its normal adult position has long been known as Sprengel's deformity. Associated with scapular deformity, frequently there are connections between the scapula and the spine which may be osseous ("omovertebral bone"), cartilaginous or ligamentous. Cervical ribs may be present in as many as 31.4 per cent of the cases and other rib abnormalities in 48.5 per cent of cases.[4] Various operative procedures[2,3,5,6,7] have been described for "undescended scapula," but, undoubtedly, that of Schrock[5,6] has been recognized most generally. Surgery is neither necessary nor desirable in every case of Sprengel's deformity; the operative indications are marked deformity, pain and limitation of motion. These have been emphasized recently by Greville and Coventry.[3]

It is to those cases, where operation is indicated and abnormal cervical ribs are present, that our attention is focused in this discussion.

The pressure produced by cervical ribs on adjacent nerves and vessels is well known. The postoperative complication of brachial paralysis in Sprengel's deformity has long been recognized. As recently as 1952 a report of this postoperative complication in 12.5 per cent of cases of Sprengel's deformity was made. In these cases various operative procedures were used to move the scapula and the shoulder caudally. No discussion of the problem of postoperative paralysis was made, except to state that attempts at overcorrection should be condemned. In 4 cases, the same author reported that no attempt was made to correct the abnormal position of the scapula. In these 4 cases surgery was restricted to bony resection of the superomedial portion of the

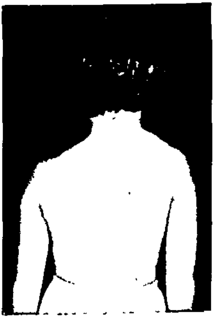


FIG 1. Nine-year-old girl with congenital elevation of the scapula, the right acromion being about 2 inches higher than the left

* Sioux Falls, South Dakota.

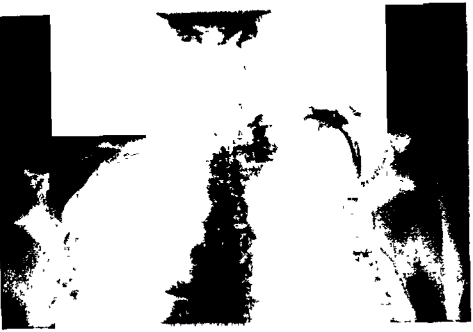


FIG. 2. Roentgenogram showing, in addition to the elevated scapula, abnormally curved and high right 1st and 2nd ribs, fusion of 4th, 5th and 6th right ribs and an upper dorsal scoliosis

scapula and excision of an omovertebral bone in 3 cases. Abduction was increased in 2 of 3 patients in whom it had been restricted before operation.

It was the opinion of one of us (R.E.V.) that the abnormal ribs in the cervical area might well be one of several factors contributing to the postoperative paralysis following transplantation of the scapula, and excision of the abnormal rib or ribs, as a preliminary procedure, was worthy of consideration. Accordingly, in 1953, it was elected to excise the abnormal ribs through a posterior incision, which later was used for transplantation of the scapula. The case is reported as follows:

CASE REPORT

The patient, a white female child of 9 years, was born with a marked deformity of the right shoulder. At the age of 5 months, a diagnosis of Sprengel's deformity had been made. Clinical examination showed a rather severe deformity of the right shoulder, the right acromion being about 2 inches (5.08 cm.) higher than the left (Fig. 1). There were visible and palpable prominences in the right supraclavicular area, and a roentgenogram (Fig. 2) showed abnormally high, curved, right first and second ribs. In addition to the elevated scapula, the fouth, fifth and sixth right ribs were fused, and a right upper dorsal scoliosis was present. No attempt had been made to correct the deformity.

It was felt that local resection of the superomedial scapula would only bring the high cervical ribs into further prominence and would not lower the acromial level (Fig. 1). In reviewing the roentgenograms (Fig. 2), it was evident that a considerable length of the brachial plexus and vessels was expended in arching upward over the abnormally high ribs; it appeared that the excision of the ribs would afford considerably more length and mobility to move the scapula downward. Accordingly, it was elected to perform a preliminary cervical rib resection, to be followed by transplantation of the scapula

The patient was admitted to the hospital on July 16, 1953, and the ribs were operated on the following day (by G.I.W.C.) under ether-nitrous oxide-oxygen anesthesia, following an induction with intravenous Pentothal Sodium.[1] Through a posterior incision, portions of the first and the second right ribs were resected subperiosteally. The operation was interrupted by a generalized convulsion and a high rectal temperature of 40° C. (104° F.). While the cause was unknown, it was speculated that it might be an ether convulsion. The wound was closed as rapidly as possible, and a small rent was torn in the pleura to cause some pneumothorax, which was treated in the usual manner. Roentgenograms [illegible] ised; [illegible] She [illegible] r the scapular transplantation within the next few weeks.

On January 5, 1954, the patient was next seen. Roentgenograms at this time showed the ribs to be reforming to such an extent that re-excision was advisable; this was done on May 28, 1954.

13

Abnormal Ribs in the Cervical Region Associated with Sprengel's Deformity

G. I. W. Cottam, M.D., F.A.C.S.,
and Robert E. VanDemark, M.D., F.A.C.S.*

Developmental failure of the scapula to descend completely to its normal adult position has long been known as Sprengel's deformity. Associated with scapular deformity, frequently there are connections between the scapula and the spine which may be osseous ("omovertebral bone"), cartilaginous or ligamentous. Cervical ribs may be present in as many as 31.4 per cent of the cases and other rib abnormalities in 48.5 per cent of cases.[4] Various operative procedures[2,3,5,6,7] have been described for "undescended scapula," but, undoubtedly, that of Schrock[5,6] has been recognized most generally. Surgery is neither necessary nor desirable in every case of Sprengel's deformity; the operative indications are marked deformity, pain and limitation of motion. These have been emphasized recently by Greville and Coventry[3]

It is to those cases, where operation is indicated and abnormal cervical ribs are present, that our attention is focused in this discussion.

The pressure produced by cervical ribs on adjacent nerves and vessels is well known. The postoperative complication of brachial paralysis in Sprengel's deformity has long been recognized As recently as 1952 a report of this postoperative complication in 12.5 per cent of cases of Sprengel's deformity was made. In these cases various operative procedures were used to move the scapula and the shoulder caudally. No discussion of the problem of postoperative paralysis was made, except to state that attempts at overcorrection should be condemned. In 4 cases, the same author reported that no attempt was made to correct the abnormal position of the scapula. In these 4 cases surgery was restricted to bony resection of the superomedial portion of the

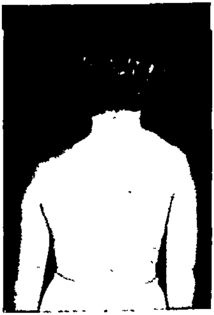


Fig. 1. Nine-year-old girl with congenital elevation of the scapula, the right acromion being about 2 inches higher than the left

* Sioux Falls, South Dakota.

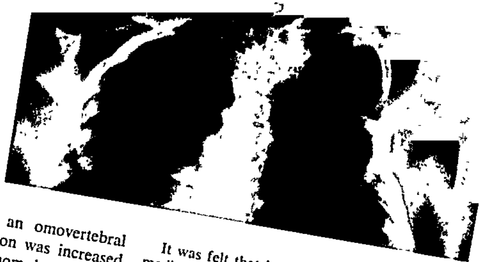


FIG. 2. Roentgenogram showing, in addition to the elevated scapula, abnormally curved and high right 1st and 2nd ribs, fusion of 4th, 5th and 6th right ribs and an upper dorsal scoliosis.

scapula and excision of an omovertebral bone in 3 cases. Abduction was increased in 2 of 3 patients in whom it had been restricted before operation.

It was the opinion of one of us (R.E.V.) that the abnormal ribs in the cervical area might well be one of several factors contributing to the postoperative paralysis following transplantation of the scapula, and excision of the abnormal rib or ribs, as a preliminary procedure, was worthy of consideration. Accordingly, in 1953, it was elected to excise the abnormal ribs through a posterior incision, which later was used for transplantation of the scapula. The case is reported as follows:

CASE REPORT

The patient, a white female child of 9 years, was born with a marked deformity of the right shoulder. At the age of 5 months, a diagnosis of Sprengel's deformity had been made. Clinical examination showed a rather severe deformity of the right shoulder, the right acromion being about 2 inches (5.08 cm.) higher than the left (Fig. 1). There were visible and palpable prominences in the right supraclavicular area, and a roentgenogram (Fig. 2) showed abnormally high, curved, right first and second ribs. In addition to the elevated scapula, the fouth, fifth and sixth right ribs were fused, and a right upper dorsal scoliosis was present. No attempt had been made to correct the deformity.

It was felt that local resection of the superomedial scapula would only bring the high cervical ribs into further prominence and would not lower the acromial level (Fig. 1). In reviewing the roentgenograms (Fig. 2), it was evident that a considerable length of the brachial plexus and vessels was expended in arching upward over the abnormally high ribs; it appeared that the excision of the ribs would afford considerably more length and mobility to move the scapula downward. Accordingly, it was elected to perform a preliminary cervical rib resection, to be followed by transplantation of the scapula.

The patient was admitted to the hospital on July 16, 1953, and the ribs were operated on the following day (by G.I.W.C.) under ether-nitrous oxide-oxygen anesthesia, following an induction with intravenous Pentothal Sodium.[1] Through a posterior incision, portions of the first and the second right ribs were resected subperiosteally. The operation was interrupted by a generalized convulsion and a high rectal temperature of 40° C. (104° F.). While the cause was unknown, it was speculated that it might be an ether convulsion. The wound was closed as rapidly as possible, and a small rent was torn in the pleura to cause some pneumothorax, which was treated in the usual manner. Roentgenograms showed the ribs to have been well excised; the patient's postoperative course was good. She left the hospital on July 29, to return for the scapular transplantation within the next few weeks.

On January 5, 1954, the patient was next seen. Roentgenograms at this time showed the ribs to be reforming to such an extent that re-excision was advisable; this was done on May 28, 1954.

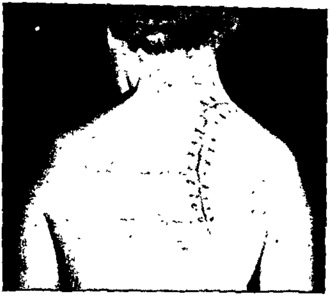


FIG. 3. Postoperative appearance of patient.

A small amount of pneumothorax occurred during the operation, which was controlled at the site. Plugging of the intratracheal tube interrupted the operative procedure temporarily. Check-up roentgenograms appeared to be good, and the patient's course was uneventful. She was dismissed from the hospital on July 6, 1954.

Following readmission to the hospital on July 8, 1954, the transplantation of the scapula was performed (by R.E.V.) according to the method of Schrock. No evidence of nerve disturbance was seen postoperatively Roentgenograms at this time showed that the elevation of the shoulder had been reduced considerably.

It has been stated that the results of treatment are better if it is carried out early, since the operation is more difficult as growth progresses, and, ultimately, the displacement becomes uncorrectable.[7] In the case presented, transplantation at 10 years was followed by definite improvement in the appearance of the shoulder (Fig. 3). The roentgenograms (Fig 4) likewise showed improvement; there was some new bone formation at the site of the previous upper margin of the scapula. Function of the shoulder is excellent in all respects.

COMMENT

Jeannopoulos stated that transplantation of the scapula is most successful in children before the age of 5 years. Preliminary cervical rib resection may increase the age limit when transplantation can be performed safely. Greville and Coventry feel that the ages of 8 to 14 years are best for resection of the prominent portions of the scapulae and the omovertebral bones. It is our opinion that, particularly in adults, resection of associated abnormal cervical ribs might be carried out optionally through the same incision in those cases with visible supraclavicular rib prominences. In this manner obvious deformity is eliminated and future complications from these ribs prevented. Resection of the superomedial scapula and the omovertebral bone is indicated particularly in older individuals with limitation of motion



FIG 4 Postoperative roentgenogram following subtotal excision of the deformed upper right ribs and transplantation of the scapula. A small strip of myositis ossificans has occurred along the previous site of the superior margin of the scapula.

due to the omovertebral bony connection with the spine. Rib excision may be performed through a posterior incision, or an anterior approach may be used. The ready reformation of excised ribs in children requires the prompt performance of the scapular transplantation. In view of the high incidence of neurologic complications following transplantation, preliminary rib excision should be seriously considered in all cases where abnormal ribs are present in the cervical region and scapular transplantation is to be performed.

REFERENCES

1. Cottam, Goeffrey: Intravenous drip anesthesia with Pentothal Sodium; report of 7,694 cases, Am. J. Surg. 76:23-28, 1948.
2. DePalma, A. F.: Surgery of the Shoulder, Philadelphia, Lippincott, 1950.
3. Greville, N. R., and Coventry, M. B.: Congenital high scapula (Sprengel's deformity), Proc. Staff Meet., Mayo Clin. 31:465-472, 1956.
4. Jeannopoulos, C. L.: Congenital elevation of the scapula, J. Bone & Joint Surg. 34A: 883-892, 1952.
5. Schrock, R. D.: Congenital abnormalities at the cervicothoracic level, *in* Am. Acad. Orthop. Surgeons Instructional Course Lectures, vol. 6, pp. 228-236, Ann Arbor, Edwards, 1949.
6. ———: Congenital elevation of the scapula, J. Bone & Joint Surg. 8:207-215, 1926.
7. Speed, J. S., and Knight, R. A. (eds.): Campbell's Operative Orthopedics, ed. 3, St. Louis, Mosby, 1956.

Anormal Costas Cervical e le Deformitate de Sprengel

Summario in Interlingua

Le deformitate de Sprengel es associate con costas cervical in 31,4 pro cento del casos. Le pression effectuate per costas cervical super le adjacente nervos e vasos es ben cognoscite. Iste pression es augmentate quando le scapula es transplantate in direction caudal. Paralyse del plexo brachial occurre possibilemente como complication post-operatori in 12,5 pro cento del casos de deformitate de Sprengel que es subjicite al transplantation del scapula. Le excision preliminari del costa o costas provide un augmentate extension e mobilitate del nervos e vasos post transplantation del scapula. In le caso hic reportate le excision preliminari del costas permitteva transplantation del scapula sin complicationes, a un etate plus avantiate que lo que es ordinarimente compatibile con tal successo. Excision de omne visibile costas cervical pare etiam recommendabile in gruppos de etate plus avantiate pro qui le excision del scapula superomedial e del osso omovertebral es le manovra de election.

14

A Destructive Lesion Involving the Intervertebral Disk in Children

S. S. MATHEWS, M.D., L. L. WILTSE, M.D., AND M. J. KARBELNIG, M.D.*

During the past several years we have observed a lesion that occurs in the intervertebral disk space in children, which we believe to be a separate clinical entity. Our findings suggest that it is definitely inflammatory in nature. The exact cause of the inflammatory process is uncertain. Seven of these cases were seen at the Children's Hospital of Los Angeles and 2 are from the private practice of one of us (L.L.W.).

A similar finding has been reported in the literature, but, thus far, we have not found a completely accurate description.

A typical case is that of a young child, 2 to 3 years of age, who is brought to the doctor complaining of pain in the back, stiffness of the back and the legs and often exhibiting a definite limp. The family gives the history that the child had been entirely well until a few days previously when he became ill with a fever and signs of an upper respiratory infection. Then, during the next few days, the back, the neck and the leg symptoms appeared.

On examination, the child is not acutely ill. The temperature is elevated only about a degree or two. Flexing the neck causes pain in the back, and straight leg raising is very limited Careful examination reveals no leg or neck muscle spasm, the only muscle spasm being in the back. Reflexes are found to be normal, and there is no demonstrable muscle weakness. It is important that the examiner differentiate voluntary abdominal splinting due to back muscle spasm from true muscle weakness. Sensation is normal. The white blood count is elevated, with a shift toward the polymorphonuclear series. The erythrocyte sedimentation rate is increased uniformly, and urinalysis is negative. Blood chemistries in those cases in which it was performed also were negative.

Roentgenograms of the spine, when taken immediately upon the start of symptoms, are entirely negative, but after about 2 weeks, a mild narrowing of 1 disk space is noted. This narrowing progresses for another few weeks, then remains stationary, and, in some cases, actually appears to reconstitute slightly. Some irregularity or fuzziness of the contiguous borders of the bony vertebrae may disappear in 3 to 4 months. All that remains is some slight to moderate sclerosis of the bone adjacent to a narrowed disk.

The child is never acutely ill, but the back may remain stiff for 3 to 5 weeks. There is often a considerable limp—the "hip joint syndrome"—but the pathology never has been demonstrated in the hip. Under adequate treatment, including rest in bed, a Bradford frame and/or a cast and antibiotics, the temperature returns to normal in about 7 to 10 days, while the sedimentation rate returns to normal in about 6 weeks. Between 2 to 3 weeks after onset, the child seems quite well and would be up and around if permitted to do so. In one case there was recurrence of

* Long Beach, California.

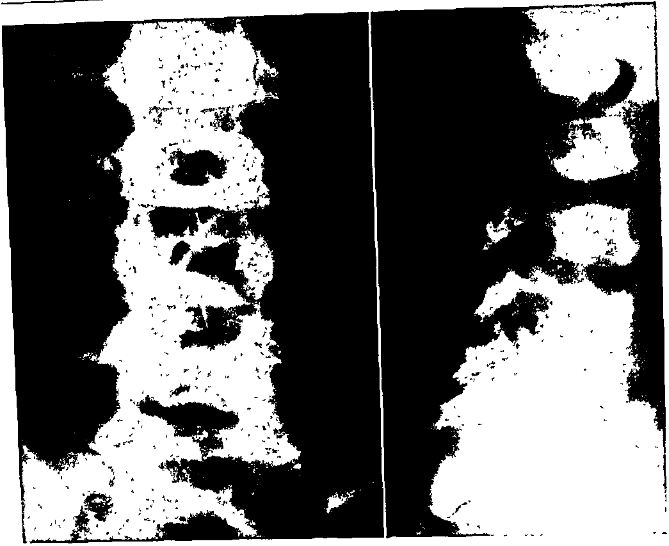


FIG. 1. See text (p. 167)

symptoms after 13 months, but a long-range follow-up of this case and all our other cases indicated that after the episode subsides the healing is complete, although the roentgenographic narrowing persists indefinitely.

REVIEW OF THE LITERATURE

In 1933, Smith[14] described a benign form of osteomyelitis of the spine with thinning of the intervertebral disk as a typical sign. He described cases in which the disk was merely thinned and some with thinning and partial destruction of the adjacent joint margins. Some of these patients went on to bony ankylosis, an occurrence which we noted in only the earliest cases (possibly because of the early use of antibiotics). Flemming[4] noted similar lesions in adults but did not include children in his series. Kulowski[9] reported on 102 cases of osteomyelitis of the spine and admitted that a more benign form had been recognized. The age span in his group was 8 to 62.

In 1940, Ghormley, Bickel and Dickson[5] discussed a condition which is probably similar to the disease entity we are presenting, but their age group (9 to 59 years) again was primarily in adults. These authors referred to the condition as "infectious spondylitis" and felt that only after extensive bone involvement occurs should it be called osteomyelitis. If only the intervertebral disk and adjacent vertebral borders were involved, then it was not a true osteomyelitis of the spine. Guri[6] and Martin[10] also reported pyogenic osteomyelitis of the spine but did mention a milder form of the disease

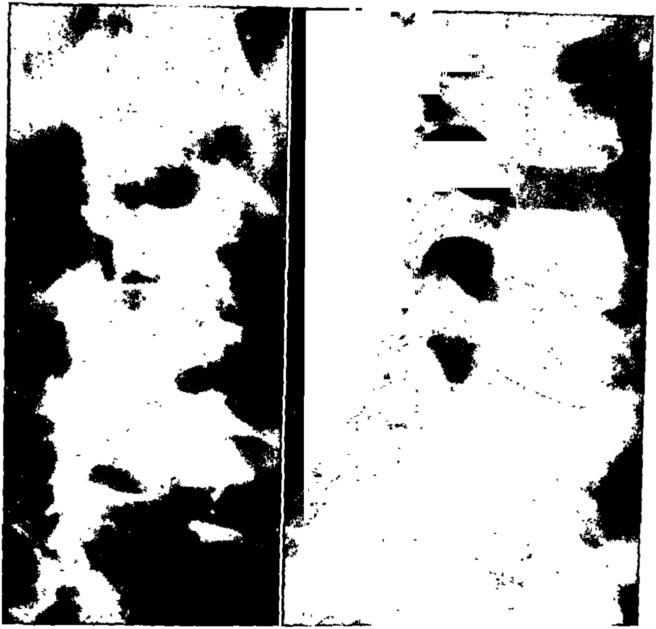


FIG. 2. See text (p. 167)

which could have been similar to the entity we are reporting.

Bremner and Neligan[1] reported 7 cases with an age span of 9 months to 2½ years, and Saenger[13] also reported a similar disease process, using the term "spondylarthritis" to describe it.

The literature review illustrates that heretofore considerable confusion existed between this condition and osteomyelitis of the vertebrae. These able investigators seem to touch all around this condition, but only the article by Saenger actually described this entity. We believe it to be a primary disease of the intervertebral disk, a distinct clinical entity, which is quite definitely infectious, possibly due to a streptococcus, although in no case was the organism isolated or identified. Our cases have led us to the conclusion that this condition is curable, that the patient recovers completely and has no further trouble unless he may have some later sequelae which might accrue from a narrowed disk.

On page 166 there is a presentation in tabular form of the 9 cases seen by us:

Our patients range from 22 months to 14 years of age and represent follow-ups from

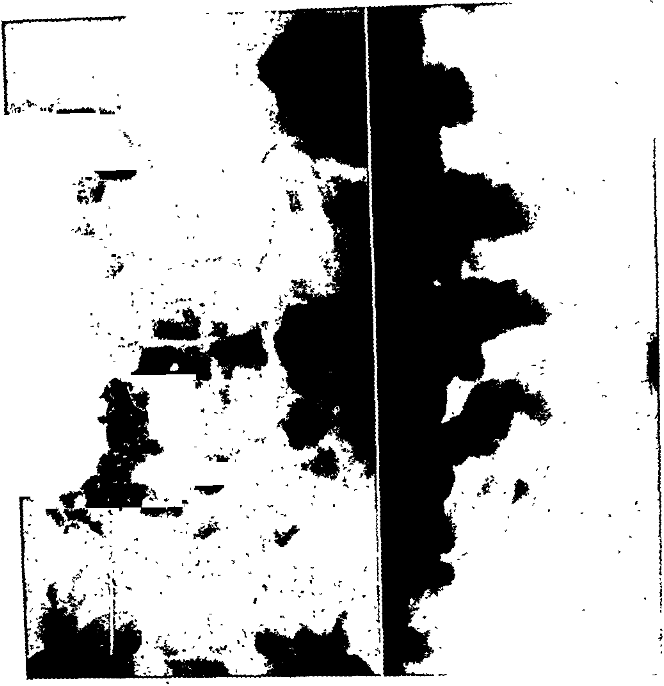


FIG. 3. See text (p. 167)

3 months to as long as 14 years from the onset of our earliest case. One of the most important facts about the condition is that the tuberculin skin tests were negative. Lumbar punctures, when done, showed normal dynamics and cellular counts. One case (T.C.) had a recurrence of an identical syndrome after 13 months, but his follow-up for 16 months since that episode has shown complete healing, as did all the others in the group. That is, each child returned to complete well-being, with only the persistent intervertebral space narrowing remaining as a stigma of this disease. One case (G.H.) went on to almost bony fusion. This patient did not receive antibiotics but did receive sulfathiazole for 1 month. Interestingly enough, another case (J.G.) did not receive antibiotics but did not go beyond mild narrowing of the disk space.

In all cases the sedimentation rate returned to normal and stayed there after a few weeks. Febrile agglutination tests, when performed, were always negative.

Summary of 9 Cases

Case No	Age at Onset	Initial Symptoms	Physical Findings	WBC (000)	PMN %	Tuberculin Skin Test	Sed. Rate Onset	Sed. Rate End of Rx	Roentgenographic Findings	Treatment	Follow-up	Condition When Last Seen
1 (D.N.)	13 yr	Severe back pain, unable to stand or sit	Pain over L-2 Back muscle spasm	12,3	61	Neg.	54	6	Narrowing L1-L2 interspace with adjacent margin destruction	Antibiotics Cast	2½ yr.	Back range of motion normal Entirely asymptomatic Roentgenograms show no change
2 (T.L.)	22 mo.	Limp Temperature	Back muscle spasm	12,2	57	Neg	64	4	Same, involving L3-L4 interspace	Antibiotics Frame Cast	16 mo.	Entirely asymptomatic Gait is normal
3 (D.B.)	2 yr.	Back muscle spasm. Limp	Back muscle spasm	11,1	33	Neg	21	9	Same, involving L3-L4 interspace	Bed rest Cast	6 yr.	Complete recovery
4 (J.G.)	2 yr.	Back and groin pain for 2 mo.	Back muscle spasm and tenderness	6,1	49	Neg	50	15	Same, involving L1-L2 interspace	Frame Cast Brace	6 yr.	Complete recovery
5 (T.C.)	3 yr.	Back pain and fever	Marked back and neck rigidity	23,	85	Neg.	36	4	L4-L3 interspace narrowing	Antibiotics Frame Cast	2 yr.	Complete recovery
6 (H.F.)	4 yr.	Pain and weakness in hips	Back muscle spasm and temperature	8,6	63	Neg	49	8	L3-L4 interspace narrowing with marginal erosion	Antibiotics Frame Cast	6 yr.	Developed a mild scoliosis 1 year after discharge
7 (G.H.)	2 yr	Limp Fever Stiff back	Back muscle spasm, listless	17,4	55	Neg.	Not done		L3-L4 interspace narrowing	Sulfathiazole Bed rest Cast	14 yr	Clinically recovered. Roentgenograms show attempt at fusion with interspace narrowing
8 (J.P.)	3 yr.	Pain in hip Stiff back Fever	Back muscle spasm. Limp	10,7	66	Neg.	44	—	L4-L5 interspace narrowing with marginal erosion	Antibiotics Cast	4 mo.	Completely well
9 (J.T.)	11 yr.	URI, pain in flank and back	Back, neck and hamstring tightness	12,3	63	Neg.	48	—	T11-T12 interspace narrowing	Antibiotics Cast	4 mo	Still in cast, but entirely asymptomatic Antistreptolysin titer markedly elevated

An interesting finding occurred in one case, the most recent, in that antistreptolysin titers were done on three occasions, once 3 weeks after the onset and again 1 week later. Both of these tests demonstrated an extremely high antistreptolysin titer. The third one, done 8 months later, showed the titer approaching normal again. In reviewing the history of this child, no streptococcic infection had occurred in her past history, and although the onset of the condition simulated an upper respiratory condition, there was no real sore throat, tonsillitis, or anything that might point to a streptococcic sore throat. It might be that this was due to hematogenous streptococcic infection of the disk. This is something which should be pursued further, as it may be the key to the true etiology of this condition.

In order that the entire picture may be better presented, roentgenograms of 2 cases are included. In Figure 1, roentgenograms of Case 8 were taken shortly after the onset of the condition. These were interpreted as negative, whereas 5 weeks after the onset of her symptoms (Fig. 2) the roentgenograms show narrowing of the L4-L5 interspace with erosions of the adjacent vertebral margins. Figure 3 illustrates the roentgenographic picture of Case 2, where the intervertebral interspace narrowing and the articular cortex erosion occurred at the L3-L4 interspace.

CONCLUSION

A disease process has been described in which a narrowing of an intervertebral disk in children occurs with or without contiguous subchondral sclerosis of bone. This disease is believed to be of infectious origin.

REFERENCES

1. Bremner, A., and Neligan, G.: A benign form of acute osteitis of the spine in young children, Brit. M. J. 1:856, 1953.
2. Butler, E., and Blusner, I.: Staphylococcal osteomyelitis of the spine, Lancet 1:480, 1941.
3. Compere, E., and Garrison, M.: Correlation of pathological and x-ray findings in tuberculous and pyogenic infections of vertebrae, Ann. Surg. 104:1038, 1936.
4. Flemming, C.: Chronic staphylococcic osteomyelitis of the spine, Proc. Roy. Soc. Med. 28:897, 1935.
5. Ghormley, R., Bickel, W. H., and Dickson, D. D.: A study of acute infectious lesions of the intervertebral disks, South. M. J. 33: 347, 1940.
6. Guri, J.: Pyogenic osteomyelitis of the spine, J. Bone & Joint Surg. 28:29, 1946.
7. Keyes, J., and Compere, E.: Normal and pathological changes in the intervertebral disk, J. Bone & Joint Surg. 14:897, 1932.
8. Knuttsson, F.: Fusion of vertebrae following a non-infectious disturbance in the zone of growth, Acta radiol. 32:404, 1949.
9. Kulowski, J.: Pyogenic osteomyelitis of the spine—102 cases, J. Bone & Joint Surg. 18:343, 1936.
10. Martin, P.: Pyogenic osteomyelitis of the spine, Brit. M. J. 2:688, 1946.
11. Nathan, L., and Kuhns, J.: Epiphysitis of the spine, J. Bone & Joint Surg. 22:1940, 1925.
12. Phemister, D. B.: Changes in articular surfaces in tuberculous and in pyogenic infections of joints, Am. J. Roentgenol. 12:1, 1924.
13. Saenger, E. L.: Spondylarthritis in children, Am. J. Roentgenol. 64:20, 1950.
14. Smith, A.: A benign form of osteomyelitis of the spine, J.A.M.A. 101:335, 1933.
15. Wilensky, A. O.: Osteomyelitis of vertebrae, Ann. Surg. 89:561, 731, 1929.

Un Lesion Destructive in le Discos Intervertebral de Infantes

Summario in Interlingua

Es reportate un serie de nove casos de lesiones destructive primari observate in le discos intervertebral de infantes. Le tableau clinic es si uniforme que illo suggere le stipulation de un sol morbo que es separate e distincte ab le osteomyelites. Illo occurre usualmente in le spina lumbar e es characterisate per un restriction progressive del

spatio del disco intervertebral e in certe casos per alicun destruction del adjacente margines ossee. Radiographias subsequente demonstra un curation progressive, sed un certe grado de restriction del interspatio persiste. Le lesion es non-tuberculotic, e le exacte etiologia remane incerte. Un del patientes habeva un elevate titro de antistreptocysina, sed nulle streptococcos esseva trovate in culturas sanguinee de tres de nostre patientes.

In le caso typic, un infante de duo o tres annos de etate disveloppa subitemente un leve grado de febre, dorsalgia, irritabilitate, e anorexia Il pote haber rigiditate solmente nuchal o rigiditate del spina integre. In certe casos on nota claudication, non associate con ulle constatationes coxal. Le reflexos e le sensation es intacte, sed il pote occurrer un certe grado de spasmo de musculo paravertebral.

Il ha leve grados de leucocytosis con deviation sinistrorse, sed le tests del urina, le *serologia, e le test cutanee a tuberculina es* omnes negative. Punctura spinal es negative. Altere tests cutanee esseva negative in omne le casos testate. Le sedimentation esseva uniformemente accelerate durante le phase active del morbo, sed in le curso del melioration clinic illo retornava a nivellos normal.

Le periodo del observation consecutori variava inter plure menses e dece-quatro annos. Le etates del patientes variava inter 22 menses e dece-quatro annos al tempore del declaration del disordine. Le curso hospitalari esseva routinari. Le patientes esseva tractate con antibioticos e allectation usque le sedimentation habeva retornate a tempores normal. In le majoritate del casos le tractamento includeva le application de un apparato gypsate. Ambulation esseva initiate quando le symptomas habeva regredite. Nulle del casos monstrava suppuration, formation de abscessos o sinos, o altere indicationes pro un intervention chirurgic.

Nos opina que iste casos representa un invasion primari del disco intervertebral a base infectiose. Le condition responde al tractamento. Si le tractamento es adequate, le condition non recurre in le casos typic. *Illo es apparentemente auto-limitante e lassa* le patiente con solmente in restringite spatio discal con un certe asperitate del adjacente superficies ossee. Il pare que il se tracta de un condition que es satis commun.

15

The Management of Idiopathic Scoliosis*

JOHN H. MOE, M.D.†

DEFINITION

When the cause of a structural lateral curvature of the spine cannot be determined, a diagnosis of idiopathic scoliosis must be made. Unsatisfactory as this terminology may be, one has no choice but to continue the use of this term, for it represents a reasonably specific entity. However, the borderlines of definition are indistinct. Many of the "typical" idiopathic patterns of curvature are found in patients having a definite history of poliomyelitis. Some of the early severely structural curves show abnormal facets at the apex of the primary curve when operative exposure is made. The presence of congenital anomalies elsewhere in the body may raise the question of their relationship to what appears to be an idiopathic curve. Likewise, on rare occasions a typical idiopathic curve pattern may be found in patients having the stigmata of neurofibromatosis.

PATTERNS OF IDIOPATHIC SCOLIOSIS

The right thoracic curve is the most common pattern. The 5th and the 12th thoracic are commonly the end vertebrae of this curve pattern, but variations include the T-4 to T-10, the T-4 to T-11, the T-6 to L-1, the T-6 to L-2, or the T-6 to L-3 pattern (Fig. 1).

The double primary curve is difficult to determine unless adequate roentgenographic studies are made at an age when the curve is just beginning. Many curves, initially right thoracic, rapidly develop structural changes in the left lumbar compensatory curve below, and by the time the patient is brought in for roentgenographic evaluation, both curves may be nearly equal in angulation, rotation and vertebral wedging. In most instances of this type, side-bending films will show the left lumbar curve to be less fixed than is the right thoracic curve (Fig. 2).

The double primary curve which leaves no doubt as to its true nature begins at the early age of from 6 to 9 years. Both curves begin simultaneously and progress equally (Fig. 3).

A left, short, upper thoracic curve combined with a much longer right thoracolumbar curve is seen occasionally. Apparently this pattern is a variant of the double primary curve, for it is always progressive, and, like the true double primary curves, both curves must be fused if correction is to be maintained.

The left thoracolumbar pattern of idiopathic scoliosis has its upper limit at the 8th to the 11th thoracic vertebra and its lower limit at the 3rd, the 4th, or the 5th lumbar segment (Fig. 4).

The infantile idiopathic curve described by J. I. P. James and by Scott and Morgan rarely has been observed in the United

---

* From the Scoliosis Service of the Gillette State Hospital for Crippled Children, St Paul, Minn, and the Division of Orthopedic Surgery, Department of Surgery, University of Minnesota.

† Professor and Director, Division of Orthopedic Surgery, Department of Surgery, University of Minnesota, Minneapolis, Minn.

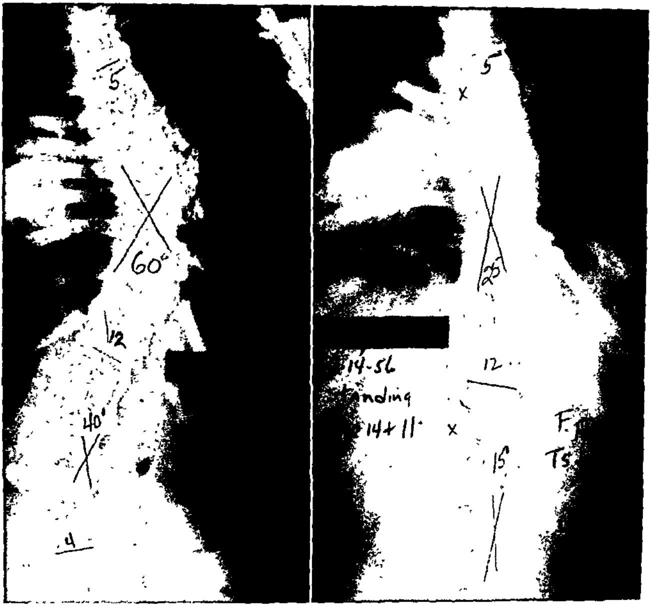


FIG. 1. The right thoracic idiopathic curve pattern. M. H., age 11 yr., 5 mo. Right curve T-5 to T-12, 60°. Maximal correction to 25°. Fusion T-5 to L-1. No loss of correction 3 years later.

States. Typically, this is a left thoracic curve noted before the age of 2 years, which was described by these authors as usually being progressive to a severe deformity. In over 500 scoliotic patients observed and treated, the author has not encountered this entity in the pattern described without evidence of congenital anomalies elsewhere.

DETERMINATION OF TREATMENT

For all practical purposes, the correction and the fusion of an idiopathic curve is done for cosmetic reasons, although, occasionally, the curve may be productive of pain Therefore, the first determination should be an evaluation of the visible deformity which the curve will produce presently or in the future.

A most important factor is the status of spinal growth, which can be charted only by noting periodically the accurate sitting and standing height of the patient. Risser has pointed out that spinal growth occurs in periodic accelerations and idiopathic curvatures normally show progression during these periods. There are many small, nondeforming curves present in adults which, no doubt, represent idiopathic curvatures

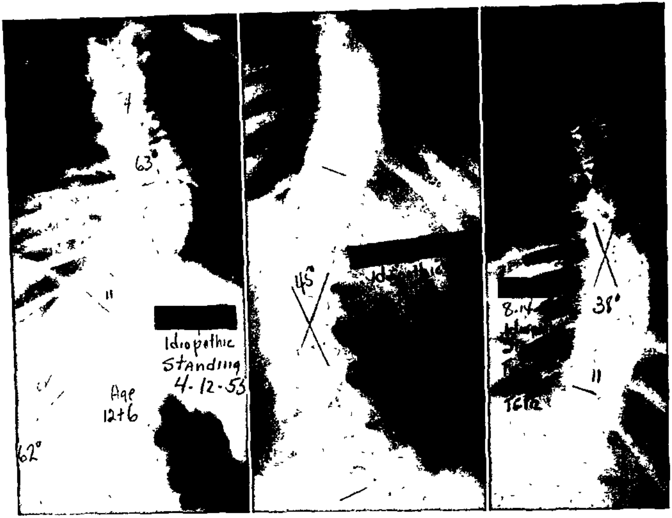


FIG. 2. The right idiopathic curve with a structural left lumbar compensation curve. M. W., age 12 yr., 6 mo. Right primary curve T-4 to T-11, 63°. T-4 and T-11 are both rotated neutrally. Lower curve T-11 to L-5 was shown to be 30° structural on left-side-bending film. Maximum correction of primary curve obtained was to 35°; therefore, fusion area selected was T-4 to T-11. Through miscounting the vertebrae at the time of fusion, the actual fusion area proved to be T-5 to T-12 (note wire markers). No harm resulted.

It is necessary to fuse only the primary curve if its end vertebrae are rotated neutrally and if the curve below has enough functional component to allow balance when maximal correction of the primary curve has been obtained

Total final correction in this patient was 25° in the primary curve plus 17° in the compensatory curve below. The advantage of limiting the fusion area to the primary curve is obvious.

that began in childhood or adolescence, which did not progress sufficiently to produce a cosmetic deformity. The author's own experience and observations have led him to agree with Risser that most idiopathic curves referred for an orthopaedic opinion in the preadolescent and early adolescent age already have progressed or will progress so that deformity is obvious. Cobb, through inclusion of all the minor curves seen in adults, has stated that 80 per cent of idiopathic curvatures do not progress to a deforming state and, therefore, only 20 per cent require correction and fusion. However, general agreement concedes that the earlier the onset of the curve the greater the ultimate deformity.

Risser has defined the sign of the iliac apophysis and has attested to its accuracy in denoting the termination of growth of the

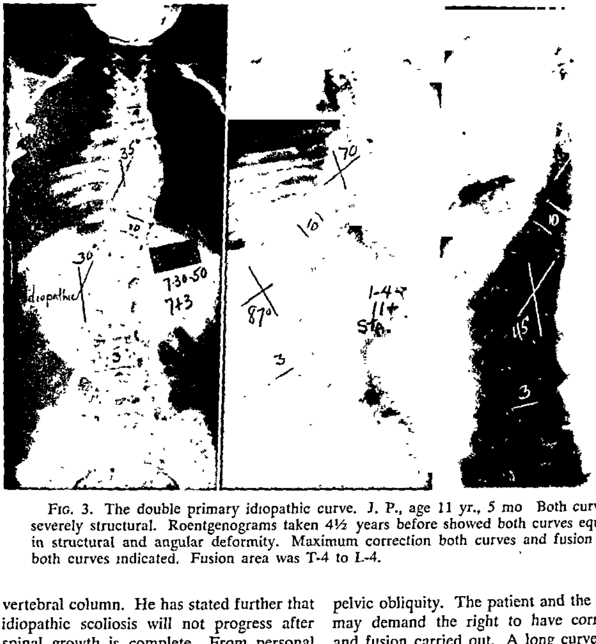


FIG. 3. The double primary idiopathic curve. J. P., age 11 yr., 5 mo Both curves severely structural. Roentgenograms taken 4½ years before showed both curves equal in structural and angular deformity. Maximum correction both curves and fusion of both curves indicated. Fusion area was T-4 to L-4.

vertebral column. He has stated further that idiopathic scoliosis will not progress after spinal growth is complete. From personal experience, these statements are essentially verified, noting only that there are occasional minor variations, such as might be shown by a 10° increase in an idiopathic curve occurring after the iliac apophyses have completed their excursion and have dipped to show contact with the posterior iliac spine. From the same experience, it may be stated that idiopathic curves do not necessarily increase until the iliac apophyses have completed their excursion.

Deformity is dependent upon the length and the location of the curve. A curvature of 35° extending from T-6 to L-5 may be accompanied by a considerable body list and pelvic obliquity. The patient and the parent may demand the right to have correction and fusion carried out. A long curve is always more deforming, for it will not permit compensation to occur within the spine itself. On the other hand, a quadruple curve, with the 2 center curves, the right thoracic and the left lumbar, balanced at 45° or 50°, often will be scarcely visible, and no treatment will be desired or indicated. The shorter the curves and the greater their number in a given spine the less the visible deformity. Ponseti and Friedman, as well as James, have pointed out that primary lumbar curves are less deforming than primary thoracic or thoracolumbar curves. Most of the lumbar curves analyzed by these authors contained only 5 vertebrae, while the

thoracolumbar curvatures were much longer.

Effective conservative cast correction must give nearly complete or preferably overcorrection of the primary curve. In the presence of structural changes in the primary curve, and more particularly in the compensatory curve, such complete correction or overcorrection is impossible; thus, conservative treatment in structural curves seldom is indicated. To be effective, cast correction must be continued over a period of many months and it must be repeated at intervals if improvement is not maintained.

Conservative efforts to control mild and relatively flexible curves also may be directed toward creating a temporary pelvic

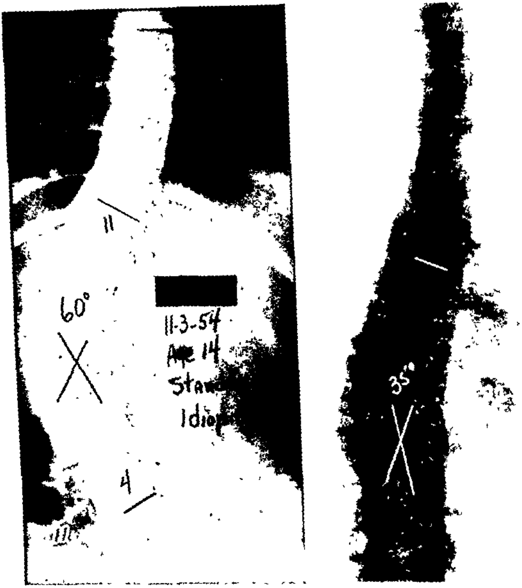


FIG 4. The left primary thoracolumbar pattern. B. Z., age 14. Left curve T-11 to L-4, 60° Iliac apophyses capping, indicating that little or no further progress could be expected Maximum correction to 30°. Initial fusion T-11 to L-4 showed pseudarthroses present 6 months postoperatively. Repair of graft defects and extension of graft to T-9 were followed by solid fusion shown by roentgenogram 9 months after the repair and the extension of the graft. Loss of correction and prolongation of immobilization were minimal, since the pseudarthrosis was discovered and reoperation performed relatively early. The fusion area planned initially should have been T-9 to L-4. Note that T-11 and T-10 are rotated and that T-9 is neutral. Also note that L-4 is rotated, but that because of its low lumbar location, fusion does not have to be extended to include neutrally rotated L-5.

obliquity by means of a shoe lift on the side of the convexity of the thoracolumbar curve. When there is leg length discrepancy, the short leg is on the side of the convexity of the primary curve; hence, it is only rational to suppose that correction of the leg length discrepancy will correct the curve if it is *functional and creating an opposite leg* length discrepancy will tend to improve it if there are mild structural changes (Fig. 5).

Decompensation of spinal curvatures is indicated by a list of the body, a tilting of the pelvis and a dropping of the shoulder. Cobb noted that the body list is always toward the side of the convexity of the primary curve, and the high side of the pelvis is always on the side of the concavity of the primary curve. Such decompensation should *be considered as a clear-cut indication for* correction and fusion of the curve. It is of great interest to note that a small amount of correction may give a marked cosmetic im-

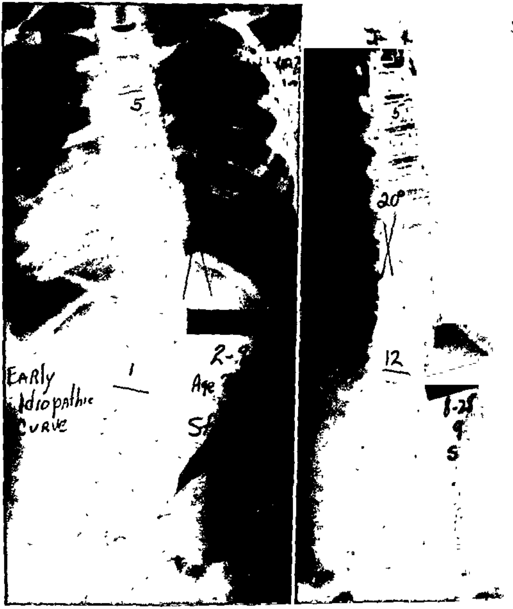


FIG. 5 Conservative measures in treatment of mild early idiopathic curves P. G., age 7 yr., 3 mo., had a mildly structural curve T-5 to L-1 right idiopathic, 25°. The right leg was minimally shorter than the left. Two and one half years later the curve was 20° and was shortened by one vertebra. Treatment during this period had been only the wearing of a ¾-inch lift on the right shoe

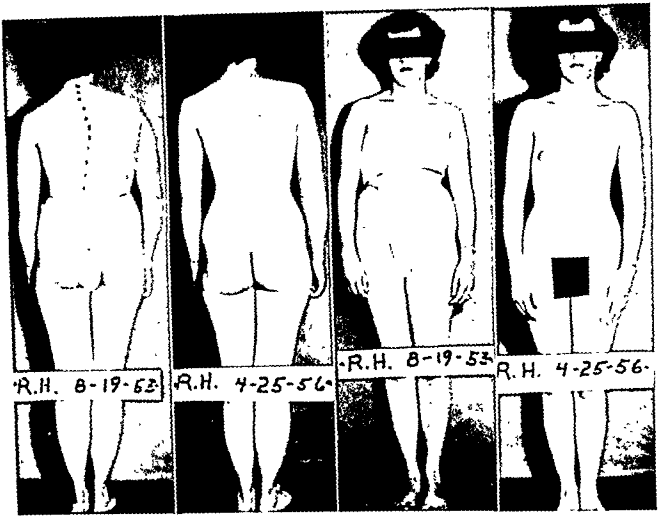
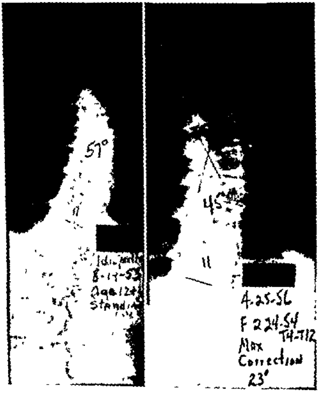


FIG. 6. The degree of cosmetic improvement is not necessarily proportional to the correction of angulation on roentgenographic measurement of the curve. In this patient the maximal correction of a 57° right idiopathic curve T-4 to T-11 was to 23°. Through failure to recognize and protect a weak fusion, a loss of 20° occurred. Nevertheless, the 12° measured gain resulted in regaining compensation completely and in a rather marked cosmetic improvement



provement through the regaining of compensation (Fig. 6).

So long as the curves are relatively flexible, there is no objection to a policy of watchful expectancy in a curve which may not progress to a cosmetic deformity by the time spinal growth is complete, for a flexible curve can be corrected when the indications for such correction are definitely established (Fig. 7)

METHODS OF CORRECTION

In the series of scoliotic patients upon which these expressed opinions are based

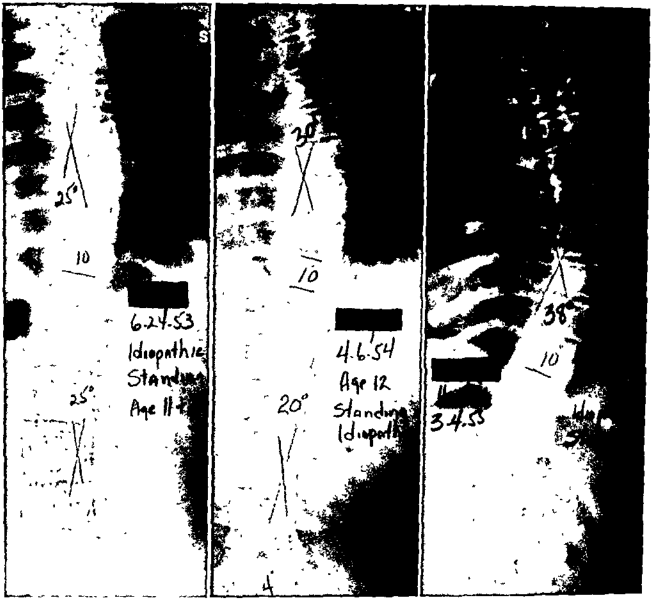


FIG. 7: A-C above; D and E on page 177. Progression of an idiopathic curve. (A, *Left)* M. S., first seen in 1953. Idiopathic curve right T-3 to T-10. Age 11 yr., 2 mo. Minimal deformity No treatment. (B, *Center)* 1954, age 12. Minimal increase in right thoracic curve Minimal deformity. No treatment. (C, *Right)* 1955, age 13. Curve increase to 38°. Cosmetic deformity becoming a problem but still not severe. Decision made to correct and fuse.

there have been 3 methods of correction used.*

1. A wedging cast was first used, applied as recommended by Cobb, with the patient first bent to the side which obtained maximal correction of the compensatory curves, a full cast being applied in this position including the neck, the head and one thigh. Hinges and turnbuckles then were inserted to correct the primary curve slowly. Later this was modified to what may be termed the "rapid wedging" cast in which the plaster is wedged immediately after it hardens, using the plaster as hinges. This rapid method proved to be as effective in most instances as the gradual correction by incorporated metal hinges and the turnbuckle.

2. The Milwaukee brace of Blount and Schmidt was used in a substantial number

* The total number of curves of all types corrected and fused to date is 338 Of these, 126 have been classified as idiopathic.

of patients. When well fitted it proved to be an excellent means of correction. The handicap first encountered in its use proved to be the inability of the brace shop to produce a well-fitting brace. More lately, the brace shop has learned to follow the instructions of Blount and Schmidt, but lack of time discourages the brace shop personnel from making very many of these braces.

3. The Risser localizer cast has been used almost exclusively during the past 3 years. It has proved to be efficient and comfortable. The resident staff very quickly learns the technic of its application.

SELECTION OF THE FUSION AREA

A distinction must be made between the measured curve and the area to be fused.

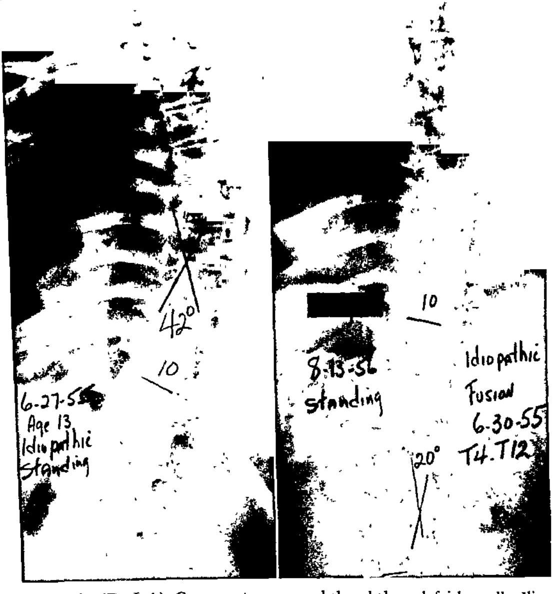


FIG. 7 (D, *Left*) Compensatory curve below balanced fairly well. Iliac apophyses not visible. (E, *Right*) Fourteen months later the curve was fused solidly at 21°, while the compensatory curve below balanced the corrected thoracic curve Correction was by Risser localizer cast. Fusion was facet method, with iliac bone added. Total correction is to 20° above and 27° below. The fusion area was planned T-3 to T-11. Through miscounting at time of operation the actual fusion area was T-4 to T-12. Since T-4 was a neutral vertebra, it was felt that no loss of correction would occur.

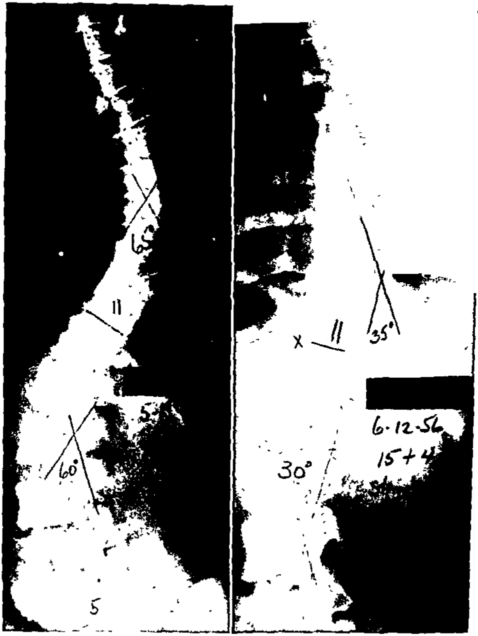


FIG. 8. Selection of fusion area. Right idiopathic curve, T-5 to T-11, 65° standing. Age of patient, 11 yr., 3 mo. T-5 and T-11 are rotated neutrally. Fusion area limited to measured primary curve. Maximum correction to 25°. Loss during plaster immobilization to 35°. Final correction 4 years after fusion 35°. Result rated excellent

The end vertebrae of the measured curve are those which show maximum tilting. In addition, the interspace above and below these vertebrae either are parallel with the end vertebrae or show a reversal of the wedging present within the curve area. Lines are drawn along the superior border of the upper end vertebra and along the inferior border of the lower end vertebra. From these lines perpendiculars which intersect are erected The angle to be measured will then be alternate or opposite to that which would be formed by the intersection of the lines drawn along the vertebral body margins. This is the method of measurement popularized by Cobb.

The rotation of the vertebral bodies is determined by the position of the oval pedicle shadows in relation to the lateral margins of the vertebral bodies. When the pedicles are equidistant from the lateral vertebral margin on either side the vertebra may be said to be in neutral rotation. When the lateral border of the body extends further beyond one pedicle than the other that vertebra may be said to be rotated. Such rotation is toward the convexity of the curve.

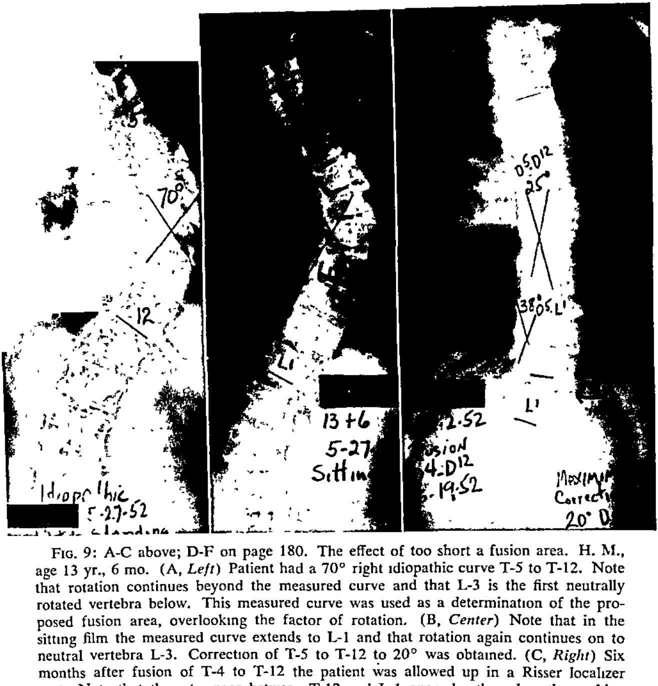


FIG. 9: A-C above; D-F on page 180. The effect of too short a fusion area. H. M., age 13 yr., 6 mo. (A, *Left*) Patient had a 70° right idiopathic curve T-5 to T-12. Note that rotation continues beyond the measured curve and that L-3 is the first neutrally rotated vertebra below. This measured curve was used as a determination of the proposed fusion area, overlooking the factor of rotation. (B, *Center*) Note that in the sitting film the measured curve extends to L-1 and that rotation again continues on to neutral vertebra L-3. Correction of T-5 to T-12 to 20° was obtained. (C, *Right*) Six months after fusion of T-4 to T-12 the patient was allowed up in a Risser localizer cast. Note that the interspace between T-12 and L-1 opened rather abruptly, making L-1 now an obvious part of the curve. T-5 to T-12 has maintained practically the maximum correction which was obtained, but the inclusion of L-1 gave an increase of over 10° of angular deformity. (The fusion was planned for T-5 to L-1, but the vertebrae were miscounted at operation, and T-4 to T-12 were fused instead. The error was not discovered immediately.)

Rotation of the vertebrae is always present in a structural curve. Such rotation may terminate with the end of the measured curve, *the end vertebrae of the curve then* being rotated neutrally. On the other hand, rotation toward the convexity may continue 1, 2, or more vertebrae below the measured end of the curve.

Several general rules may be followed in *determining the length of the fusion area.*

1. A right thoracic idiopathic curve in which the end vertebrae of the measured

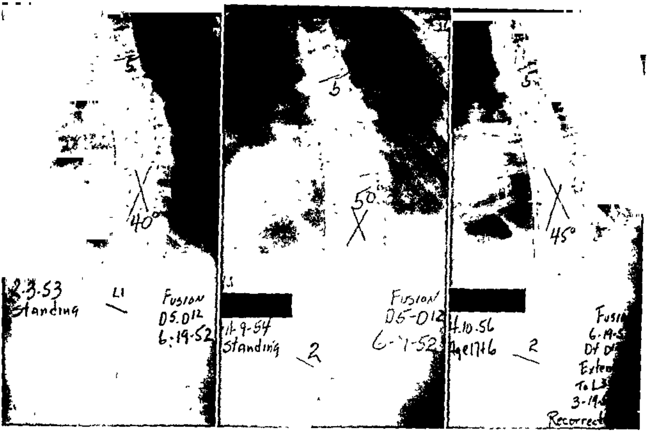


FIG. 9. (D, *Left*) Progression of deformity continued, the patient finding it difficult to make a decision to undergo further surgery. (E, *Center*) Increase in deformity now was marked, and still another vertebra has been added below to the curve. The patient now decided to undergo an attempt at recorrection and extension of the fusion. (F, *Right*) Recorrection to 35° was obtained by means of the Risser localizer cast, and on March 19, 1955, the fusion was extended to include T-3 and L-3. A solid fusion was noted a year later with some improvement in the amount of angular deformity.

curve are rotated neutrally requires only fusion of the curve. A second necessity for such a short fusion area is a sufficient functional element in the compensatory lumbar curve below, as shown on the left side-bending roentgenogram, to allow balance with the amount of correction which has been obtained in the right thoracic curve (Fig. 8).

2. In a right thoracic idiopathic curve, if rotation toward the convexity of the curve continues beyond the measured curve, the fusion area must be extended beyond the measured curve to include all of the rotated vertebrae and usually the first neutrally rotated vertebra as well. "Fusing short" in this type of curve will result in loss of correction through the addition of the rotated vertebrae below to the measured curve (Fig 9).

Where rotation continues beyond the measured curve, not only the precorrection roentgenogram but the correction film also must be evaluated. It is generally true that the fusion area must include all of the rotated vertebrae and also the neutral end vertebrae as seen on the precorrection film. It is also true that the area may be shortened if the "rotational lag" is eliminated and the primary curve is shortened in the correction film Shortening of the fusion area in this circumstance must never be by more than 1, or, at the most, 2 vertebrae. The long-established rule of "fusion from parallel vertebra to parallel vertebra" is to be remembered in dealing with these problems (Fig. 10).

3. In thoracic curves where the end vertebrae of the measured curves also are

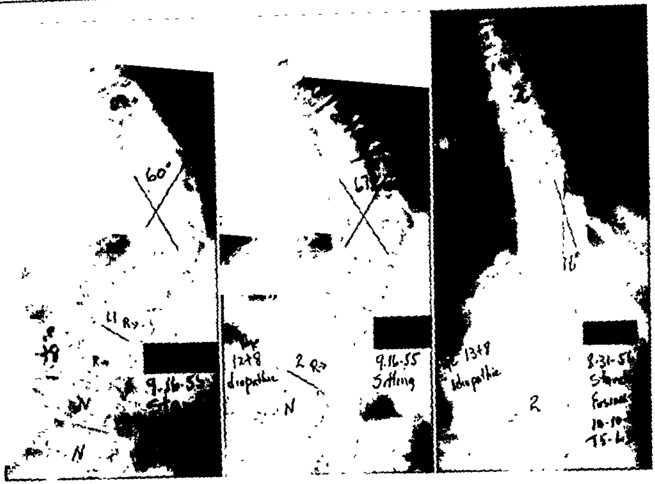


FIG. 10. Selection of fusion area. P. J., age 12 yr., 8 mo. Right idiopathic curve T-6 to L-1 standing, T-6 to L-2 sitting. L-1 and L-2 are rotated. L-3 is neutral. Fusion area selected T-5 to L-3. Full amount of correction maintained. Because of derotation occurring with correction, a fusion area of T-5 to L-2 probably would have given an equally satisfactory outcome.

rotated neutrally, the fusion area can be extended above and below the measured curve without particular harm to the patient, provided that balanced correction is being carried out in the Risser localizer cast or in the Milwaukee brace (Fig. 11).

4. The younger the patient the more certain one must be to fuse long enough. When in doubt, add a vertebra to the fusion area.

5. In a left lumbar primary curve, where the measured curve extends to the 3rd or the 4th lumbar vertebra and where rotation continues beyond the measured curve so that the neutral vertebra is L-5 or even S-1, the fusion area need not include the neutrally rotated vertebrae below but usually can be limited to the measured curve. The lower the curve extends the more one can disregard rotation. In the author's experience, it has not been found necessary to fuse to the sacrum in any idiopathic curve (Fig. 4).

6. The double primary curve should have both curves fused in their entirety. The short left high thoracic curve with the long right thoracolumbar curve (a variant of the double primary curve) also should have both curves fused in their entirety (Fig. 3).

THE PROPER AGE FOR FUSION

Most patients with idiopathic curves present themselves for treatment at ages between 11 and 14 years. In this age group there should be no hesitation whatever to recommend correction and fusion if this is indicated.

Also, in patients younger than this age group, progressive curves should be treated by correction and fusion. The production of a deforming lordosis by the fusion has not been observed in the author's experience,

although a slight reduction in the anteroposterior diameter of the thorax has been observed very occasionally. If a thoracic lordosis is already present before fusion, it will not be improved by the operation and it may progress somewhat following surgery. The presence of a very narrow anteroposterior diameter of the chest with a very flat or lordotic thoracic spine, in a child of 10 years or younger should constitute a contraindication to immediate fusion, since the curve can be kept from progressing by means of the Risser localizer cast until the child is older.

CAUSES FOR FAILURES AND POOR RESULTS

The most common reason for failure to maintain correction of a fused curve is the presence of a pseudarthrosis in the graft.

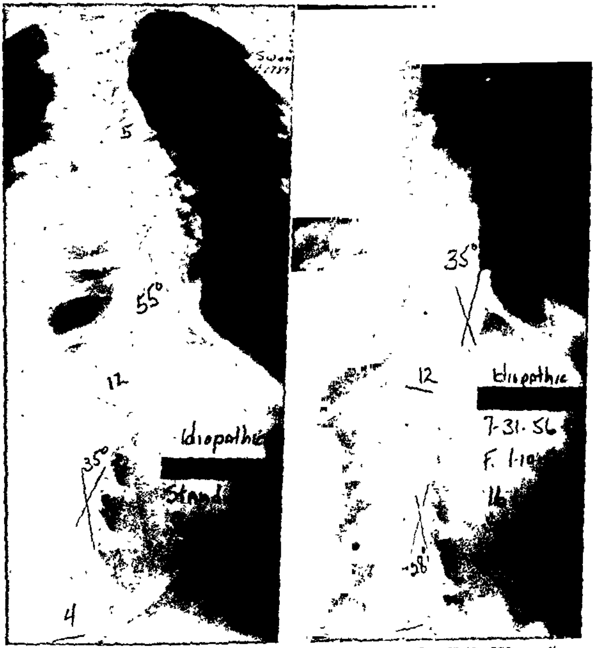


FIG. 11 C. S., age 13 yr., 1 mo Right idiopathic curve T-5 to T-12, 55° standing. T-5 and T-12 are rotated neutrally. Iliac apophyses not visible. Fusion area was T-4 to L-1. Maximal correction to 30°. Final correction 3 years after fusion 35°. Fusion of only the measured curve T-5 to T-12 would have given equally good results, but extending the fusion area did no harm.

In the author's initial experience, the incidence of pseudarthroses was over 50 per cent—a most discouraging percentage. Loss of correction occurred because of failure to diagnose the defect. As time went on a more careful search was made for defects in the graft by repeated roentgenographic studies, particularly in the oblique views. Side-bending films were used occasionally but seldom were found to be necessary. Improvement in the surgical technic of fusion, particularly the institution of a meticulous facet fusion, helped lessen the incidence of pseudarthroses so that at the present time a solid fusion can be expected to occur in 85 to 90 per cent of idiopathic curves operated on under the author's supervision.

Pseudarthroses are uncommon in the thoracic spine above T-11. The highest incidence has been found to be in the T-12—L-1 interspace and in the lumbar spine below. It has been found advantageous to add iliac bone to the facet fusion below the T-11 area.

Another cause for loss of correction in idiopathic scoliosis is too short a fusion area. This has been discussed already in a preceding paragraph.

A third cause for loss of correction is failure to protect an immature fusion area for a sufficient period of time. The time required for firm and mature fixation of the curve varies from 8 months to over a year. As a rule, younger children can be allowed out of the corrective cast or brace earlier than older children. The roentgenographic appearance of the fusion area is of utmost importance. No questionable fusion should be allowed to go without adequate protection Clearly evident pseudarthroses should be explored surgically and repaired when the cast is changed 5 to 6 months after the fusion has been performed.

On an average, the author's experience, the patient with idiopathic scoliosis remains supine in the operative cast for 5 months postfusion. Then the cast is removed, right and left oblique and anteroposterior roentgenograms are taken, and the status of the fusion is evaluated. A new Risser localizer cast is applied, and the patient is allowed to become ambulatory if the fusion has a good appearance. The patient returns in 3 months for cast removal and further roentgenographic evaluation of the fusion area. If all is well, a short cast is applied and is worn for an additional period of 2 months. This cast fits snugly over the trunk but does not include the neck.

DISCUSSION

No field in orthopaedic surgery offers more challenge to the orthopaedist than does the treatment of scoliosis. In no other field are the rewards greater for good results than those expressed in the gratitude and the happiness of the patient and the parent. It is hoped that the present trend toward a co-operative effort on the part of those who are seeing and treating scoliotics in large numbers will lead to a better understanding of the fundamental concepts of scoliosis and to the formulation of recognized principles of treatment which can be accepted everywhere. The opinions expressed in the foregoing paragraphs are those gained from personal association with the recognized authorities on scoliosis: Cobb, Risser, Blount, Schmidt and others. These opinions have proved to be sound and workable in the author's experience, and it is hoped that they will be of help to others who struggle with this difficult problem.

BIBLIOGRAPHY

Blount, W. P., and Schmidt, A. C.: The Milwaukee Brace, 1953, and subsequent mimeographed data published privately.

Cobb, J. R.: Personal communication

———: Technique, after-treatment and results of spine fusion for scoliosis *in* Am. Acad. Orthop. Surgeons Instructional Course Lectures, vol. 9, p. 65, Ann Arbor, Edwards, 1952.

James, J. I. P.: Idiopathic scoliosis; the prognosis, diagnosis and operative indications related to curve patterns and the age at onset, J. Bone & Joint Surg. 36B:36, 1954.

———: Kyphoscoliosis, J. Bone & Joint Surg. 37B:414, 1955.

———: Two curve patterns in idiopathic structural scoliosis, J. Bone & Joint Surg. 33B:399, 1951.

Ponseti, I. V., and Friedman, B.: Changes in the scoliotic spine after fusion, J. Bone & Joint Surg. 32A:751, 1950.

———: Prognosis in idiopathic scoliosis, J. Bone & Joint Surg. 32A:381, 1950.

Risser, J. C., Lauder, C. H., Norquies, D. N., and Craig, W. A.: Three types of body casts *in* Am. Acad. Orthop. Surgeons Instructional Course Lectures, vol. 10, p. 131, Ann Arbor, Edwards, 1953.

Schmidt, A. C.: Fundamental Principles and Treatment of Scoliosis, Lectures on Orthopaedics and the Rheumatic Diseases, Dedication Volume, The Hospital for Special Surgery, pp. 87-101, New Haven, Conn., Quinnipiack Press, Inc., 1956.

Tractamento de Scoliosis Idiopathic

Summario in Interlingua

Scoliosis idiopathic require mesuras corrective principalmente pro rationes cosmetic. Le majoritate del patientes qui es presentate al orthopedista exhibi o va disveloppar grados sufficientemente pronunciate de deformitate pro justificar correction e fusion. Le deformitate depende in grande mesura del loco e del extension del curva. Correction conservative per medio del apparato localisante de Risser es efficace in casos de curvatura pauco pronunciate e flexibile, sed curvas structural de grado moderate o sever deberea esser tractate per correction e fusion le plus promptemente possibile. In iste tractamento, le etate del patiente non deberea esser considerate como un obstaculo. Certe regulas pote determinar le longor del area de fusion. Le correction es melio obtenite per medio del apparato localisante de Risser o del supporto Milwaukee. Non-mantenentia del correction resulta quasi exclusivemente del presentia de pseudoarthroses in le graffo, de non protegite graffos immatur, o de un non satis longe area de fusion.

16

Wire Loop in Arthrodesis of the Shoulder*

ROBERT E. CARROLL, M.D.

In reconstruction of the upper extremity, control of the shoulder joint is mandatory for function of the extremity as a whole. When sufficient musculature is missing, the control is obtained by an arthrodesis of the humeral head to the scapula at the glenoid process. It is of the utmost importance that the proper position or angle of bony union be obtained. This is difficult, as the relationship of 3 phases must be understood. The purpose of the author in this chapter is to suggest a simple method by which the proper position may be obtained following the operation for arthrodesis of the shoulder.

The importance of the position of the arm following operation is emphasized by Steindler.[3] He has pointed out the importance of function obtained by forward flexion and external rotation of the arm, as well as the degree of abduction. Key[2] points out that a good result from shoulder arthrodesis is relatively difficult to obtain unless the larger head of the humerus is held firmly against the smaller surface of the glenoid or fixed to the scapula in other ways. He points out that the plaster spica is difficult to apply following the operation when the patient is still relaxed under general anesthesia. In 1942, a Research Committee of the American Orthopaedic Association[1] made a study of shoulder arthrodesis. It was their finding that a relatively large proportion of the cases studied would have been better if more attention had been given to precise positioning of the arm following operation. At the end of an operation, the patient usually is supine on the table. He is swathed copiously with drapes which do not allow easy palpation of the entire scapula and the upper extremity. If the body is tilted by sandbags the true planes may not be recognized and considered. In studying arthrodesis of the shoulder, the author has been impressed by the fact that the measured angle in the postoperative roentgenogram frequently is far different from that estimated by the surgeon in his report of the operation.

Innumerable methods are proposed for fixation of the shoulder to promote arthrodesis. With careful technic, solid union is obtained. In general, more difficulty is experienced with obtaining the proper planes of position. Most of the procedures use rigid fixation of the humeral head to the scapula. This may be in the form of bone—such as a graft, a block or a strut. In other procedures, the fixation is held rigidly by metal pins, screws or nails. These methods have one defect in common. They do not permit any change in position once the operation is finished and the plaster cast applied. The operation described in this paper permits a change of position without loss of coaptation in the glenohumeral junction.

PROCEDURE FOR OPERATION

The patient is placed on the table in the supine position. A fracture table with a canvas sling that can be tightened and also removed is much preferred. A small pillow

* From the New York Orthopaedic Hospital at the Columbia-Presbyterian Medical Center, New York, N. Y.

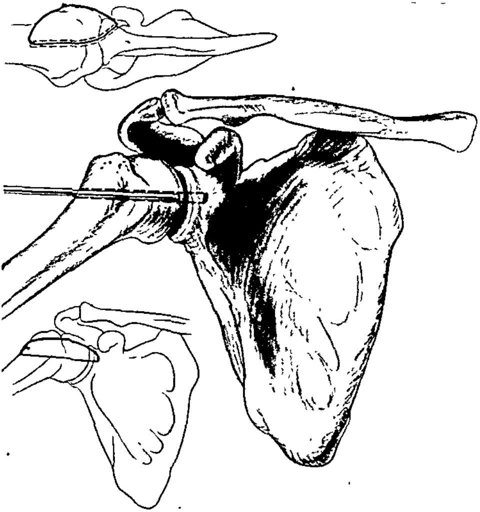


FIG. 1. A tunnel is made with a gouge through the head of the humerus and anterior superior lip of the glenoid process A wire is passed through these holes and tied over the anterior surface of the joint.



or a folded sheet is placed under the scapula and the hip of the side to be operated on The upper extremity is draped free so that it can be moved about during the operation.

With the arm at rest in a neutral position, the skin incision is made over the lateral aspect of the shoulder. This incision starts in the area of the trapezius insertion and curves anterior to the acromial process. Then it is brought posteriorly over the deltoid area This produces a flat or open semicircle. The deltoid can be identified through this curved incision. The origin of the del-

FIG 2. The wire loop passes through the head of the humerus and the anterior superior lip of the glenoid process This fixation holds the bones together firmly while the plaster spica is applied. Moreover, it permits a change in the plane of position following operation without loss of coaptation.

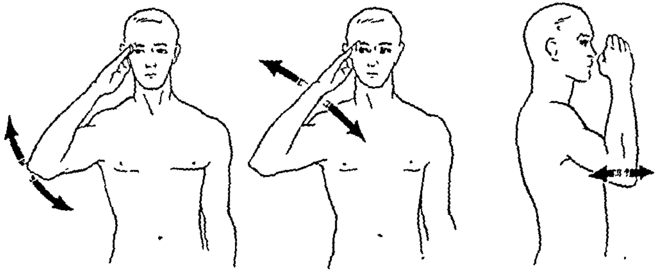


FIG. 3. The functional position for arthrodesis of the shoulder approximates the position of salute. With a wire loop fixation, changes may be made postoperatively in each of the three planes—abduction, external rotation and forward flexion.

toid is dissected free from the acromial process. Then a longitudinal incision is made distally along the shaft of the humerus to complete the T-shaped opening. Further dissection will free the legs of the T. The deltoid can be dissected anteriorly along the lateral clavicle and laid back. With a scissors, the capsule is excised and discarded. At this time the long head of the biceps muscle should be transplanted to the coracoid process and short head of the biceps if it seems necessary to preserve the power. The glenoid labrum is dissected free by the scalpel and discarded.

The next step is to remove all articular cartilage from the glenoid fossa. Long-handled osteotomes and gouges are especially useful here. The surface is left with roughened cancellous bone in all quadrants. Then the arm is brought to the proposed position of arthrodesis. It is easy to see how much of the surface and the amount of articular cartilage on the head of the humerus that must be removed This is removed by means of curved osteotomes, leaving a roughened surface of cancellous bone. Next, the undersurface of the acromial process is denuded of cortex. With a curved osteotome, the acromial process is fractured as it leaves the scapula. This will permit the acromial process to be folded down in closing the wound.

Then the position of arthrodesis is chosen, and the arm is held in this position. The direction of a hole in the head of the humerus can be selected. With a stout hand gouge, a hole is made through the cortex of the humerus into the shoulder joint. The aim is roughly toward the anterior and superior quadrant of the glenoid. It is not necessary to be accurate. Then the gouge is withdrawn. Using the same gouge or a curved gouge, the hole is made through the anterior, superior lip of the glenoid process, emerging beneath the coracoid process. Care must be taken not to lever the gouge but to use it with a twisting or a screwing method. Next, a No. 22 gauge wire is then passed through the opening in the head of the humerus and on through the hole in the glenoid process (Fig. 1). Avoid sawing the wire back and forth in placing it through the holes in the bone. The two ends of the wire are then brought together over the anterior shoulder joint and are tied together firmly. The head of the humerus should sit snugly in the glenoid fossa. Additional bone is not necessary, but it can be packed around the joint if so desired.

The wound is closed by suturing the deltoid fascia to the insertion of the trapezius.



FIG. 4. Solid union has been obtained in 3 to 4 months, although a postoperative manipulation may have been done. *(Left)* Anteroposterior view. *(Right)* Axillary lateral view. These roentgenograms show the position of the wire loop used in this procedure.

If so desired, the fractured acromial process may be wired into the humeral head; however, this is not necessary to secure the arthrodesis. The acromial process is fractured so that the closing sutures will draw it down into a rounded position over the humerus and give a more natural appearance to the shoulder. A plaster spica is applied with the patient lying on the canvas sling (Fig. 2). The plaster should extend to the hand, with a support for the palm

POSTOPERATIVE MANAGEMENT

The wound can be inspected by a window in the shoulder section of the plaster spica. When pain subsides, a postoperative roentgenogram should be ordered. Usually this is in the 2nd week after surgery. The film is obtained with the patient in the standing position. The film must include the entire scapula and the proximal humerus. The desired planes can be ascertained from the roentgenogram and the clinical position of the extremity of the standing patient. If a change is desired in one or more planes, it can be obtained The patient is given a mild anodyne With a motor saw, a ring is cut in the plaster cast at the junction of the arm and the torso. The upper extremity can be moved for correction in 3 planes (Fig. 3). The eccentric position of the wire loop permits abduction, forward flexion and external rotation. The head of the humerus is held against the glenoid. Then the rent in the spica is sealed. This cast is maintained for 3 months. At that time, roentgenograms of the joint are taken to be sure that union has matured enough to allow removal of the cast.

CLINICAL EXPERIENCE

This type of arthrodesis has been used in 15 cases. The length of time that they have been followed extends from 1 year to 5 years and 3 months. All have obtained solid bony union between the 3rd and the 4th month after operation (Fig. 4) This operation was done in the process of upper extremity reconstruction for paralysis resulting from poliomyelitis or obstetric palsy. However, on one case the operation was used to arrest a joint tuberculosis.

In 5 cases the shoulder was manipulated, and the position changed after operation.

One patient required 2 sessions of positional change to obtain the desired placement. In the other 4 patients, a single change was satisfactory. No difficulty was obtained in changing the position in any plane. It was not particularly painful for the patient. The position of the humeral head in the glenoid fossa was maintained. Solid fusion was obtained between the 3rd and the 4th month following operation.

Caution is advised against placing the loop of wire across the neck of the glenoid fossa and the head of the humerus in a transverse manner. One colleague did this in performing an operation for arthrodesis of the shoulder. Excellent and firm position of the humeral head against the glenoid fossa can be obtained; however, the transverse fixation of the glenoid will permit a change only in the angle of abduction.

SUMMARY

1. In arthrodesis of the shoulder joint, a method of fixation of the humeral head to the glenoid fossa with a wire loop is presented.

2. This procedure allows revision of the planes in the postoperative state without loss in the relationship of the humeral head to the glenoid fossa.

3. Fifteen patients have been helped by this method with no failure of fusion.

REFERENCES

1. Barr, J. S., Freiberg, J. A., Colonna, P. C., and Pemberton, P. A.: A survey of end results on stabilization of the paralytic shoulder, J. Bone & Joint Surg. 24:699-707, 1942.
2. Key, J. A.: Arthrodesis of the shoulder *in* Am. Acad. Orthop. Surgeons Instructional Course Lectures, vol. 2, pp. 376-380, Ann Arbor, Edwards, 1944.
3. Steindler, A.: *Ibid.*, pp. 293-301.

17

Prosthetics in Child Amputees*

Milo B. Brooks, M.D., and Robert Mazet, Jr., M.D.

In recent years prosthetic† progress has resulted in significant improvement in prosthetic practice for the adult amputee. The availability of better devices has stimulated interest in the more or less neglected problems related to the child amputee. For all practical purposes, only in the past 30 years has any particular effort been directed toward fitting the child amputee, and then only by isolated individuals. The initial attempts in this field were mostly the responses of prosthetists to the anxious importunities of a parent that something be done.[9,13]

Perhaps because child amputees demanding attention appeared nowhere in large numbers, perhaps because of the greater urgency of trying to help adults presenting prosthetic problems, perhaps because our prostheses were too crude to inflict on children, medicine and the prosthetic industry were long content to tell parent and child to wait until growth was attained before fitting was attempted

The improved prosthetic devices and technics which have evolved in the past 10 years have coincided with interdisciplinary efforts on the part of engineers, surgeons, psychiatrists, physical and occupational therapists and prosthetists to develop prosthetic technics applicable to the child amputee.[1,2,4,5,7,10,12,13]

The most significant of these pioneering clinical studies has been that of the Juvenile Training Center of the Michigan Crippled Children's Commission.[1,2,5,6,12,14] Prior to the inception of this project, a gradual trend toward the fitting of younger children with lower extremity prostheses had taken place. Most authorities now concur that children should be fitted as soon as they commence to stand. The Michigan group has revolutionized our ideas as to when the upper extremity child amputee should be fitted. They have felt for some time that fitting should be done before the child enters kindergarten in order that he may become accustomed to prosthetic wearing before his introduction into the enlarged world of the classroom More recently they have been fitting patients as young as 8 months with passive prosthetic devices.[6] Lambert reports fitting one child of 22 months.[8]

The Michigan group has demonstrated certain fundamental tenets for successful fitting of children, which have been confirmed by our experience.

1. The team approach is essential.
2. The parents and the child must be psychologically prepared prior to prosthetic fitting.
3. An adequate postfitting program of prosthetic training is necessary.
4. Follow-up at 3-to-6-month periods is an important adjuvant.
5. The co-operation of parents and teachers in the program is necessary.
6. The prosthesis must provide comfort and function.

* From the Departments of Pediatrics and Surgery (Orthopaedic), School of Medicine, University of California Los Angeles, Cal.

† "Prosthetic" is used here to include those problems related to the medical treatment of patients, procurement and checkout of the prosthesis, training in its use and all indicated follow-up care.

Kessler[7] has stated that group meetings for parents are valuable.

THE AMPUTEE PROGRAM

The Child Amputee Prosthetics Program at the University of California, Los Angeles,* is a joint venture of the Medical School and the College of Engineering. The medical problems of each patient are investigated and prescribed for by the Medical School. Technical and engineering problems relating to the development and the fabrication of prostheses and special prosthetic devices are the province of the Prosthetics Laboratory of the College of Engineering. The disciplines within the Medical School which are participating actively in this venture are Orthopaedics, Pediatrics, Psychiatry, Social Service and Physical Therapy. Other specialties such as Roentgenology, Dermatology, Urology, Plastic Surgery, Neurosurgery, etc., are asked to see patients when problems arise within their particular specialty. The minimum requirements for a well-functioning prosthetic team are: patient and parents, physician, prosthetist and amputee trainer.

New patients initially are given a general work-up in pediatrics. Next, they and their parents are interviewed by the psychologist and the social service worker. The purpose and the modus operandi are explained by the administrator of the program. Roentgenograms and other indicated laboratory work or consultation with other medical specialties, if indicated, are secured.

Then the patient is seen in the Amputation Conference. Here the orthopaedic surgeon, the pediatrician, the engineer, the psychologist, the prosthetist, the amputee trainer and the social service worker consider the various aspects of the case If preprosthetic physical therapy or other therapy is indicated, it is prescribed If the patient is ready for prosthetic prescription, such is made. The prescribed device is fabricated, then checked for fit and function, and training in its use is instituted. The child is followed by the group at regular intervals. Records are kept on the efficiency and the use of the prosthesis, the psychological acceptance by patient, family and friends and the physiologic effects of its use. Mechanical difficulties are corrected, and new devices are prescribed as indicated. The majority of the patients are referred by the California Crippled Children's Services. Others come through physicians, prosthetists or other hospitals.

* Supported by a grant from the Children's Bureau, Department of Health, Education and Welfare, administered through the California State Bureau of Crippled Children's Services.

SURGERY OF THE CONGENITALLY DEFORMED EXTREMITY

Birch-Jensen[3] has made an exhaustive study of congenital deficiencies of the upper extremity in Denmark, classifying these according to the anatomic defects observed. He advances some theories as to etiology and divides the deformities into (1) an exogenous group, which he believes to be true spontaneous amputation, and (2) an endogenous group, which he believes to be due to disturbances in the development of the limb.

We have divided the deformities into 2 principal types for purposes of surgical consideration and for fitting.

1. The uncomplicated group is that in which there is absence of a distal segment of greater or lesser magnitude, with normal or perhaps slightly underdeveloped elements of the extremity proximal to the defect (Birch-Jensen's exogenous group). In instances of this type surgery is rarely necessary. Fitting is dependent on the level of amputation and the age of the patient. The type of prosthesis indicated for the various levels is formalized[10] to a certain extent. The factor of the patient's age is discussed below. The traumatic amputee is included in this group for prosthetic purposes, since the fitting problems are identical.

2. The second, or complicated group, is that in which all sorts of grotesque malformations may be present (Birch-Jensen's endogenous group). The distal portion of

the extremity may be fairly normal anatomically and functionally but is more likely to be only partially complete. A finger, a toe, a hand, a foot, a wrist, a forearm, leg bones and other bones may be missing, with accompanying combinations of muscle anomalies of divers types. Frequently, there is maldevelopment, with limitation of function, of a shoulder or a hip joint. These are much more difficult problems. They may require surgical extirpation of a distal segment which cannot be fitted without employing some awkward prosthetic apparatus. It may be impossible to fit the part without irritation by the prosthesis. The deformity may produce profound psychological disturbance, particularly in the teenage child. If deformities are not too severe, surgical reconstruction sometimes results in functioning extremities not requiring prostheses.[11]

Young children invariably make the maximum use of their appendage, be this little or much. In infants we do not know the growth potential of their extremities. Impaired joint function, particularly of hip or shoulder, may be improved by training. Similarly, muscular control over these joints may be increased significantly by training. Aitken and Frantz[1] have stressed the desirability of maintaining the epiphyseal growth areas in these involved extremities. In any event, growth in the affected member will lag. By preserving whatever growth potential they possess and by allowing maximum development, a better functioning part probably will result, if only because of a longer lever to activate the prosthesis better by the time puberty arrives. Then it may be feasible to fuse a knee or an elbow, amputate below the fusion area and give the child a better functioning stump than he would have had if earlier amputation had been performed.

In general, we do not advise surgery in these individuals until the overwhelming desire not to be different from others is induced by the self-consciousness of puberty. Occasionally, if a deformed distal part is extremely unsightly, functionless, or interferes markedly with prosthetic fitting, ablation may be suggested at an earlier age.

Except in rare instances of extensive bilateral involvement, we believe cineplasty should be postponed until the child is about 15 years old. By this time he will have had a fair trial of prosthetic wearing, he will have had an opportunity to see and to talk to others on whom cineplasty has been done, his muscular development will be fairly complete, he will have analyzed his own problems and will have developed some judgment.

The phocomelus, in which there is a flipperlike appendage usually close to the body, is an exaggerated example of a complicated type of deformity. These are highly individual problems about which we can express no general recommendations.

The following case reports represent typical problems of fitting, training and adjustment to prosthetic wearing encountered in our study.

CASE REPORTS

Case I. G. C., a 14-year-old left-handed boy, sustained a traumatic right wrist disarticulation as a result of a home chemical explosion 1 year before being seen in June, 1953 (Fig. 1 A & B). He was a shy, introverted and dejected boy who tended to avoid social contacts. A prosthetic device with an interchangeable APRL* hand and a No. 5 hook was furnished, and initial training was given him. At first, he tended to hide the deformity and the prosthesis and became more introverted than ever. Understanding and patience on the part of the trainer and the psychologist, plus parental help, resulted in a gradual change in his outlook. He became interested in social activities and in using his artificial hand. Some self-consciousness remained. He wore the hand at all times except for occasional work around the house, when he used the hook.

When last seen, 32 months after the first fitting, he was a good prosthetic user, he wore his device at all times, he played the violin in the school orchestra, using a specially devised

*Army Prosthetic Research Laboratory.

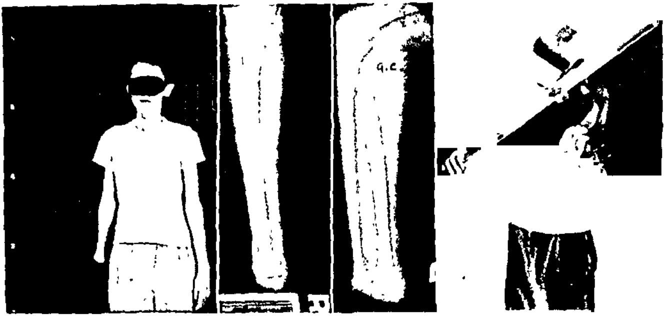


Fig. 1, Case 1. *(A, Left)* Right wrist disarticulation. *(B, Center)* Roentgenogram showing this to be an anatomic wrist disarticulation. *(C, Right)* Same patient playing violin with APRL hand and special bow holder.

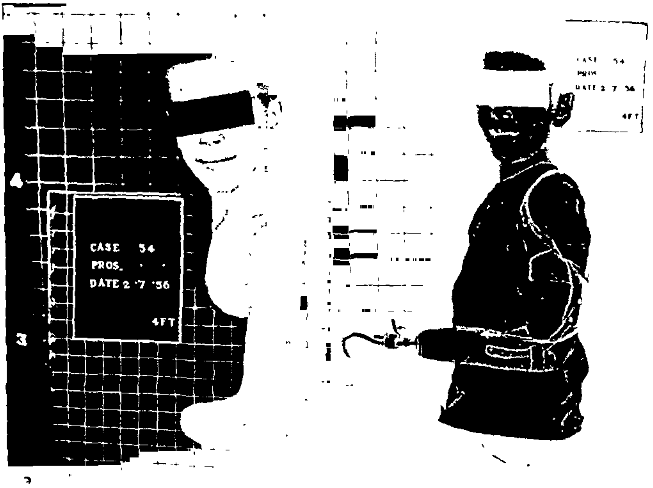


Fig. 2, Case 2. *(A, Left)* Short below-elbow amputation. *(B, Right)* Patient wearing standard short below-elbow prosthesis.

bow-holder, and was manager of his high school basketball team (Fig. 1 C).

This is an instance of anatomic wrist disarticulation which presented no unusual prosthetic problem. It illustrates the feasibility of functional fitting at this level. It also demonstrates the necessity for understanding on the part of the parents, the trainer and the psychological counselor in converting a withdrawn individual into an integrated member of society.

Case 2. M. B., an 8½-year-old boy, was first seen in March, 1955, 5 months after an automobile accident which resulted in a short left below-elbow amputation (Fig. 2 A). The patient is a resident of a small town and was a markedly confused child. Following his accident, he had been, while hospitalized, the center of attention. After discharge from the hospital this condition no longer pertained. He was not able to understand the sudden withdrawal of attention from himself and the indifference with which his contemporaries regarded his loss. He had obtained a satisfactory standard below-elbow prosthesis elsewhere and had been referred to us for training (Fig. 2 B).

Several training periods were held during his initial stay with us. He quickly learned to understand the function and the manner of use of his device. Upon his return to school he was subjected to the repetitious questions of schoolmates, and, because he could not do many of the things he had performed previously, he became withdrawn, belligerent and resentful. In consequence, his schoolwork suffered, and his parents were at a complete loss for a solution to his behavior problem.

In his small home community psychological counseling was not available. Therefore, it was necessary for him to visit us on several subsequent occasions for psychotherapy and for some additional training in prosthetic use

Ten months after his first visit there had been a considerable improvement in his attitude toward the world; he was much less antisocial, his work in school had improved, and his relations with his contemporaries were much more amicable. He is still under treatment.

This case presented a standard uncomplicated below-elbow fitting problem. It was complicated by a very definite post-traumatic psychological disturbance which necessitated considerable therapy and is not entirely resolved.

Case 3. D. B., an 8½-year-old boy, with a congenital right very short below-elbow am-

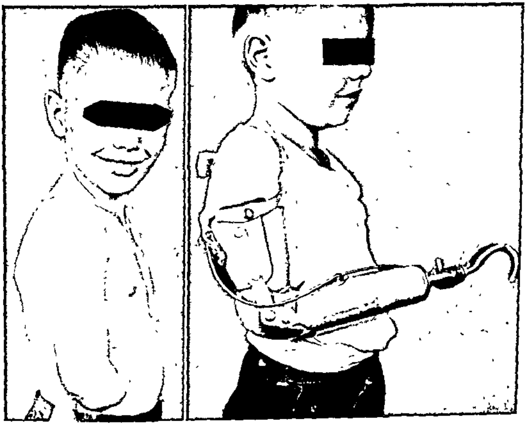


FIG 3, ꞉ 3 *(A, Left)* Very short below-elbow amputation. *(B, Right)* Patient wearing split-socket prosthesis with step-up hinge



FIG. 4, Case 4. *(A, Left)* Standard above-elbow amputation. *(B, Right)* Patient wearing standard above-elbow prosthesis.

putation (Fig. 3 A), was fitted about 2 years ago. His right ulna was 1½ inches long. He wore his first very short below-elbow prosthesis with a split socket and step-up hinge (Fig. 3 B) for 18 months before a replacement was needed because of wear and breakage. He wore it almost continuously from the beginning, in spite of rather brief initial training. Its usefulness in riding a bicycle seemed to furnish a strong incentive or "selling" factor. Following additional training 9 months after fitting, he learned much more about the usefulness of the device. He requested a change from an 88X hook to a 555X so that he could climb trees better.

This case illustrates the ease and the feasibility of fitting a prosthesis on the frequently seen very short below-elbow amputation and emphasizes the point that in the upper extremity there are no "sites of election" for amputation. With modern prosthetic skill and components, highly satisfactory fittings can be made at almost any level of amputation.

Case 4. C. D., a 13-year-old boy, was first seen in March, 1954. He had a standard left above-elbow amputation (Fig. 4 A) sustained at the age of 7, when he fell from a tree and suffered an infected open fracture of the wrist. Humeral overgrowth necessitated 2 stump revisions. He was given a standard above-elbow prosthesis with a No. 5 hook (Fig. 4 B). He received relatively little training beyond the initial checkout. When seen 19 months later, he started more active training. He seemed to be a natural wearer but did not realize the potential uses of his prosthesis. With supplementary training, plus associated adjustments of the harness and the prosthesis, he became more adept, cutting with a knife and a fork, using the telephone, dressing himself, etc. He wears his prosthesis most of the time and finds it particularly valuable in daily home deliveries of the morning paper.

He states that he can do everything without his prosthesis but does things twice as well with it. Two years after the initial fitting, he is an excellent user. He presents an example of an uncomplicated standard above-elbow amputee type and of the humeral overgrowth which sometimes occurs.

Case 5. J. R., a 4-month-old boy, was first seen in September, 1955. He had a congenital defect of the right hand and a shortened forearm segment which was bowed toward the flexor surface 90° (Fig. 5 A). Distal to this was a small soft tissue mass representing the vestigial hand, consisting of a single element with about 45° flexion and no extension. Roentgenograms showed a bowing of the forearm bones; no calcified shadows were visible distal to the wrist. A passive infant hand was prescribed (Fig. 5 B).

Several short periods of training were given the child and his mother. Two months later he was wearing the prosthesis for short periods in the morning and the afternoon and was actively



FIG. 5, Case 5. *(A, Left)* Congenital deformity of right upper extremity in 4-month-old child. *(B, Right)* Patient wearing prosthesis with infant passive hand.

using the device at play to push and pull. At 8 months he was wearing the prosthesis almost constantly during waking hours. At 10 months he had outgrown the prosthesis and required a new fitting.

In viewing the anatomic situation, it was recommended that no surgery be done at the present time, although it might be advisable



FIG. 6, Case 6. *(A, Left)* Congenital absence of left upper extremity and rudimentary right upper extremity. *(B, Right)* Patient wearing standard left-shoulder disarticulation and right above-elbow prostheses.

later to osteotomize the forearm bones and straighten them. He still uses the prosthesis continuously and indicates his desire to have it replaced when it is taken off.

This child represents our exploration of the minimum age for optimum fitting and has demonstrated that a simple, passive hand can be useful at an early age. The child seems to be developing a concept of identifying himself with his prosthesis.

The complicated cases which follow represent our efforts to help these badly handicapped individuals. They are not able to obtain as much function from their artificial extremities as the uncomplicated amputees. We think that we have helped them, but many problems in this group are still unsolved.

Case 6. D. U., an 8-year-old boy, was first seen in January, 1953. He was a congenital left-shoulder disarticulation and right-shoulder upper-extremity-with-flipper amputee (Fig. 6 A). Function of the shoulders was much restricted. A roentgenogram showed absence of normal glenohumeral articulations. He was fitted with a left shoulder-disarticulation prosthesis and a right standard above-elbow prosthesis (Fig. 6 B) with No. 88 hooks. This fitting was done in one of the prosthetic schools then in progress. No training was provided. Consequently, there was practically no prosthetic function.

He was seen in the Amputation Conference 2 years later when he was 10 years old. New prostheses with No. 555 hooks were prescribed. His agility and independence without the prostheses necessitated his having to be convinced that prosthetic function would be beneficial to him.

He was quite independent, well-adjusted, self-reliant and good in his schoolwork. He used his feet for almost everything and he refused all pity. There was no apparent psychological problem with this child. However, the mother had a guilt complex. She was a somewhat high-strung individual but she had sufficient insight to desire prosthetic training for the boy. At first the school authorities did not permit him to wear the artificial extremities at play. The mother co-operated in the training program despite her feeling of guilt. Co-operation of the school authorities also was secured.

Gradually the boy became a good prosthetic wearer despite the magnitude of his deformities He wears his devices constantly, using them at school, for eating, dressing, telephoning and in many everyday activities. Numerous minor adjustments of the prostheses and the harness have been necessary during the child's prolonged period of training. He was, by reason of his initial independence of prostheses, a challenging training problem. He illustrates the necessity of an adequate training program, the desirability of readily available prosthetic service and the benefit derived from the co-operation of school authorities.

Case 7. R. H., a 9-year-old boy, who, 2½ years before his first appearance at the Prosthetic Conference in November, 1953, had been run over by a railroad train. As a result, he presented an amputation of the right upper extremity through the surgical neck of the humerus, a right hip disarticulation and a left below-knee amputation with 4 inches of tibia (Fig. 7 A). Lower extremity prostheses had been provided elsewhere. The right was a modified saucer-type device with a shoulder strap. The left was a standard below-knee device. The right humeral segment had good strength, and there was unimpaired shoulder motion. A shoulder-disarticulation-type prosthesis was provided (Fig. 7 B).

This patient, despite intermittent training due to transportation difficulties and his multiple disabilities, has made an excellent psychological adjustment, with the help of a rather remarkable mother who has many other distressing family burdens.

He obtains surprisingly good function from his upper-extremity device which is, prosthetically, a shoulder disarticulation. He walks quite well, considering the fact that he has no right lower extremity.

Twenty-eight months after his initial visit he had outgrown the lower-extremity prostheses. His new ones have been ordered. His principal difficulty was an inability to wear his artificial arm for more than 4 hours because of excessive perspiration. The necessity for a large shoulder cap in his device further reduces the already much curtailed body surface through which this boy can perspire, thereby compounding his difficulties. This is an instance in which a courageous youngster, with the help of an understanding parent, has attained independence despite multiple amputations sustained at the age of 7

Case 8. R. G., a 6-year-old girl, presents a congenital bilateral humeral type of phocomelia. She also has an asymptomatic heart defect (Fig. 8 A & B). She was first seen in March, 1955. A standard above-elbow prosthesis

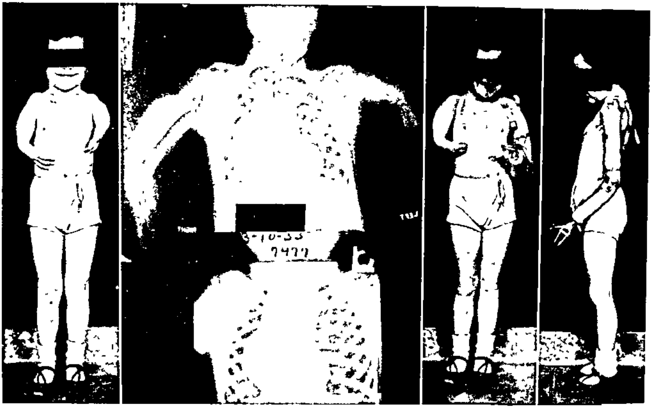


FIG. 8, Case 8. *(A, Left)* Bilateral phocomelias of upper extremities *(B, Center)* Roentgenograms showing congenital cardiac enlargement and rudimentary bone structure of extremities. *(C, Right)* Patient wearing left modified above-elbow prosthesis with cutout for vestigial hand.

on the left, which was the shorter appendage (Fig. 8 C), was prescribed, leaving the longer (right) extremity to continue its useful but limited functions. The fingers on the left appendage were utilized to operate the elbow-locking device from inside the upper shell. A cutout on the anteromedial side of the socket permits some function of the vestigial hand.

When seen after 6 months, she had had 25 training sessions. She was wearing the left prosthesis at school, and this side was becoming dominant. The muscles of the shoulder had developed noticeably. The question arose as to whether she should be fitted with a right prosthesis at this time, but it was decided to continue with 1 prosthesis until greater skill had been acquired. A new and lighter one was prescribed to allow for the growth that had taken place. Because of this short lapse in training and because of chafing of the axilla loop, the prosthesis was not worn for a brief time, and her progress regressed materially.

A year following the fitting she attends regular parochial school. Her adjustment seems to be quite adequate. A visit to her school by the project trainer was helpful in her school adjustment.

This case represents our attempt to approach the problems of the complicated group of phocomelias, for whom little help has been available in the past.

Case 9. D. F., an amazing 6-year-old girl, was born with no lower extremities and standard bilateral above-elbow amputations (Fig. 9 A & B). Her extremely well-developed torso presents a statuesque appearance. When first seen at 5 years of age she already had learned to ambulate with great dexterity by simple pelvic rotation. She was fitted with bilateral standard above-elbow prostheses (Fig. 9 C). With patient training and conscientious support of her parents, she achieved some dexterity. However, for some time she tended to concentrate on the right prosthesis and ignore the left.

After 6 months of training and use of the

FIG. 9, Case 9. *(A, Top, left)* Absence of lower extremities and bilateral above-elbow amputations *(B, Top, right)* Roentgenogram showing absence of femora and short humeri. *(C, Bottom, left)* Patient wearing bilateral above-elbow prostheses. *(D, Bottom, right)* Patient in bucket type lower extremity pylons.



FIGURE 9 (*Caption on facing page*)

upper extremities, she expressed a desire for something with which to walk. Realizing that all walking must be accomplished with pelvic rotation only, a bucket-type device strapped firmly to the pelvis with rather short pylons that could accommodate shoes was constructed (Fig. 9 D). This gives her a great amount of self-confidence and pride and permits her to "walk" across the room with relative ease.

She attends a school for the handicapped, is able to hold a book and turn the pages, write on the blackboard. She assists, although not completely, in feeding herself. She would be able to get out of her lower prostheses and into a chair and back into her prostheses alone were it not for the danger of falling.

She is a very bright, co-operative, persistent and happy girl, who, with understanding parental help, should be able to progress. This is an instance in which we were able to provide some help with a distressing problem. (She was fitted recently with Canadian hip disarticulation type prostheses.)

SURGERY IN THE TRAUMATIC AMPUTEE

Provided that the post-traumatic surgery results in a good stump with normal sensation and adequate bone covering by skin and soft tissue, subsequent surgery often is unnecessary. The placement of the scar is rarely of any significance. Spurs or neuroma should be removed only in those instances when prosthetic wearing causes pain. In some instances the fibula and the humerus will exhibit overgrowth as compared with soft tissues and will have to be cut back (Case 4). This tendency of fibula to overgrowth has long been recognized, and it is recommended that at the time of amputation it be cut 2 to 3 inches proximal to the tibia.

We should like to emphasize that there are no "sites of election" in the upper extremity.[10] All possible length at every level should be preserved. Even a half inch may add significant leverage. Satisfactory prosthetic fitting of the wrist and elbow regions is not difficult with the devices now available.

PROSTHETIC FITTING

As stated above, in the uncomplicated amputee the fitting problems are well understood, and beyond the age of 4 we have an adequate armamentarium to meet most of the functional needs of these patients (Cases 1, 2, 3 and 4).

In the younger children, neuromuscular co-ordination for prosthetic function by the amputee is not yet fully developed. Therefore, the prosthesis must be tailored to the developmental stage of the individual. When the infant is about a year old he wants to stand and will do so if he is given something to stand on. Initially, a jointless leg is probably best, with the addition of an ankle as soon as the child has good balance and commences walking At about 3 years, a knee joint may be added.

Upper extremity function is more complicated. Before the age of 1 year, the child will be able to push and pull and can profitably use the infant passive hand (Case 5). He cannot yet purposefully activate a hook or an elbow lock. A small hook can be used profitably by the child at about 2½ years, and the elbow lock and the manual wrist-rotation unit at approximately 3½ years. When he is four, usually he can use a prosthesis with all its functioning components. However, it is well to remember that the child demands *comfort* and *function*. When these are provided he will use the device. If not, he will discard it.

In the complicated type, the ingenuity of the prosthetist, the trainer and the surgeon often is taxed severely. One can readily fit an artificial arm on these children or fit the stump into an artificial leg. However, any lessened function of the shoulder seriously impairs function of the arm. Impaired hip function limits the function of the entire extremity. The difficulties of providing functioning prostheses are compounded if there is a markedly deformed partial hand or foot at the end of the extremity, or if the condition is bilateral. In some instances of upper extremity involvement, a special cutout on the sides of the device can be provided to accommodate the deformity (Case 8). It may be feasible to use a segment of this type to activate the elbow lock.

In the lower extremity, when much shortening is present, incorporation of the foot in the socket in marked equinus with some heel-bearing is often helpful, or the commonly employed extension-type prosthesis with weight-bearing on a normally positioned foot can be used. This is cosmetically undesirable, but functional; and when growth has been attained, ablation of the deformed distal portion of this extremity probably will be indicated.

TRAINING

Previous articles in this field have emphasized the necessity for an adequate training program. The Michigan group advocates an in-training program. We have been operating an outpatient program. This has proved to be disadvantageous for some of the children who live at a distance from the Medical Center. We have been strongly impressed that sporadic periods of training, interrupted by long intervals of sometimes inadequate parental supervision, are detrimental to the best prosthetic function.

Training must be highly individualized to meet the needs of the specific patient. In the infant, its limitations are determined by the physiologic development of the patient (Case 5). His attention span is limited, his co-ordination is undeveloped. He is difficult to motivate. He needs supervised periodic training for years. Changing training technics must be employed as his prosthetic device is modified to accommodate the increasing neuromuscular co-ordination of the developing child.

In lower extremity amputees, training is rarely a serious problem. Children will walk and run on an artificial limb if they can. Those under 3 may not be able to control a knee joint. Older children with short above-knee stumps may have to learn to flex the thigh rather than swing the pelvis in advancing the prosthesis. Most children need some initial help in stair climbing and in learning to fall properly. Ordinarily, a few lessons are sufficient.

In the uncomplicated groups of amputees, where there is unimpaired function of the member proximal to the level of amputation, training, in the absence of psychological complications, usually is accomplished readily unless the child is a short, bilateral, above-elbow or a shoulder-disarticulation amputee. These children can be easily shown the proper method of activating and controlling the component parts of the artificial extremity. The bilateral amputee is immediately dependent on the artificial extremities and, therefore, is sufficiently motivated to translate this knowledge into useful prosthetic function. The unilateral amputee is less dependent on his prosthesis, as has been stated previously. He will utilize the remaining portion of the amputated extremity to the best possible advantage without the artificial member. In the lower extremity, invariably he welcomes a device which will permit more facile ambulation. In the upper extremity, he must be convinced that prosthetic wearing is profitable to him (Cases 3 and 4).

We have observed that there are several types of individuals who may eschew prosthetic wearing. These are:

1. Children in the negativistic stage of development, about 2 years of age.
2. The child with an amputation at or distal to the junction of the lower and the middle thirds of the forearm, who has considerable function in the incomplete member, plus tactile sensation.
3. The older child, who over a period of years, has learned to compensate for his handicap and maintains that he can do without an artificial arm everything that he can do with it.
4. The child who has absorbed from his parents an attitude of concealing his deformity rather than seeking an adjuvant device which will permit increased function.

In these groups the training is a much more difficult problem Understanding and inventiveness on the part of the trainer and some psychiatric assistance frequently are necessary.

In the complicated group, the training

also, of necessity, must be highly individualized. The trainer must work within the physical and the emotional capacities of the patient, always seeking for means which will motivate him to greater effort (Cases 6, 7, 8 and 9). No general program can be laid out to fit all of the cases.

PSYCHOLOGICAL ASPECTS

The psychological impact of the loss of all or a portion of an extremity on the child and on the parents has not been stressed sufficiently. One of the most fruitful aspects of our program is the psychological study of this group of people. We have recognized the presence of a psychological impact but we have been surprised at the depth of this wound.

The congenital amputee very early learns to think of himself without his missing extremity. He forms an amputated self-image. The longer this attitude of mind continues, the more difficult it is for him to change and to think of using an artificial limb This is a strong argument for early prosthetic fitting. This is demonstrated further by the infant who cries to have his arm or leg returned to him when it is removed even for a short time.

The guilt feelings of a parent and his desire to hide the deformity or the prosthesis may be transferred subtly to the child and contribute subconsciously to his resistance in accepting the prosthesis The younger the child, the more susceptible he is to parental moods For this reason, we encourage families to seek counsel and aid from the prosthetic team soon after the birth of a deformed child, even though a prescription will not be contemplated for some months.

Recently we have instituted small group training classes for children with comparable deformities, we believe that this creates a salubrious atmosphere which contributes to motivation toward better prosthetic function. The patients become less self-conscious. They are stimulated and compete with one another to improve the use of the device. We have also aided the parents in organizing a group for the discussion of mutual problems and what can be done to solve them. This is definitely beneficial to the parents and indirectly beneficial to the children.

Prosthetic function is dependent not only on the level of amputation but also on the enthusiasm and the determination which the patient exhibits in obtaining maximum function from his artificial extremity. Fitting of the traumatic amputee occurs relatively soon after the physical loss and the attendant psychological trauma. He may need some time to adjust and an understanding prosthetic team to counsel and guide him, one which is not anxious to hurry him prematurely into a prosthesis.

A child's attitude and acceptance of his prosthesis is often a mirror of a parent's feelings and attitudes. An uninterested parent, who is not convinced that prosthetic wearing is helpful to the child developmentally and physically, can negate all the efforts of the best prosthetic team. Conversely, a parent who co-operates in the training program at home can contribute significantly to efficient use of the new device (Cases 1 and 7). The attitude of school authorities toward a child's wearing his prosthesis and using it to maximum advantage in school also can be either very helpful or definitely detrimental (Case 6).

In most instances, the school authorities have acquiesced readily to the suggestion that following prosthetic fitting the device and the manner of its function be demonstrated to schoolmates. This aids in acceptance of the prosthesis by playmates, lessens curiosity and obviates repetitious questioning of the wearer.

REPAIR AND REPLACEMENT

Function, and therefore, prosthetic wearing, is largely dependent on the proper condition and the fit of the artificial extremity. In active boys the devices frequently are

subjected to hard usage. Ankle bolts and bumpers may give way. Repeated wetting makes rubber feet desirable. Cables and screws in artificial arms need frequent replacement. Promptly available reparative facilities must be provided.

With our present technics, growth necessitates replacement of sockets at approximately yearly intervals.

SUMMARY

The study, the fitting and the training of 95 children with various types of amputation, congenital and traumatic, have disclosed several definite facts:

1. Children can be fitted successfully at a much earlier age than generally has been believed, i.e., under a year.
2. The psychological effects of amputation on the child and the parents are of much greater magnitude than was realized. Psychotherapy may be indicated. The child who is not prepared mentally should not be forced into a prosthesis.
3. A definitive training program for teaching the best use of these devices to children is essential. The understanding and the active co-operation of parents, school authorities and playmates are very valuable aids to good function. Discussion groups for parents should be encouraged.
4. Follow-up visits at regular intervals are mandatory to assure the proper fit and operation of the artificial member, to recheck the condition of the stump, to encourage maximum use by the patient, to stimulate the patient and the parents and to provide indicated therapy for the patient or repairs and replacements of the prosthesis.
5. A conservative attitude toward surgery is urged. In most cases little or no surgery is indicated before puberty. Except in rare instances of bilateral involvement of upper extremities, cineplasty is not advised before the 15th year and then only for carefully selected individuals. When surgery is undertaken, growth centers should be preserved, if possible. All possible length should be preserved at every level.
6. The prosthesis must provide comfort and function.
7. Best results are accomplished through prosthetic team effort.
8. Scale-down models of adult prosthetic devices are not entirely satisfactory for children. Special devices are needed.
9. A small-sized hand (now being developed) is a necessary requirement for adolescent girls.

Two areas demanding immediate investigation are now being explored by the project. The first is the development of a material which will permit remolding of the socket to accommodate growth. The second is finding a porous substance which will obviate the accumulation of perspiration within the socket.

Contributions to the care and the management of these cases by the following members of the project are gratefully acknowledged: Harry Campbell, C.P., Prosthetist; Jeanine Dennis, B.A., Amputee Trainer; Wilma Gurney, M.A., Social Worker; Gerald Gwynn, Engineer; G. F. Harland, B.S., Project Administrator; Robert Jones, B.A., Engineer; Murray Kahane, Ph.D., Psychologist; Craig L. Taylor, Ph.D., Engineer.

REFERENCES

1. Aitken, G. T., and Frantz, C. H.: The juvenile amputee, J. Bone & Joint Surg. 35A:659, 1953.
2. ———: Prostheses for the juvenile amputee, A.M.A. Am. J. Dis. Child. 89:137, 1955.
3. Birch-Jensen, A.: Congenital Defects of the Upper Extremity, Copenhagen, Munksgaard, 1949.
4. Chittenden, R. F.: The use of prosthesis for limb defects in children, Am. J. Surg. 86:128, 1953.
5. Frantz, C. H.: Child amputees can be rehabilitated, Children 3:61, 1956.
6. ———: Prosthetic problems in the juvenile amputee, Orthop & Prosthet Appl. J. 6:12, 1952.
7. Kessler, H. H.: The management of congenital amputations, Proc. Kessler Inst. for Rehab. 1:28, 1953.

8. Lambert, C. N.: Upper extremity prosthesis in the juvenile amputee, J. Bone & Joint Surg. 38A:421, 1956.
9. Langdale-Kelham, R. D.: Two decades of limbmakers, Crippled Child 21:58, 1943.
10. Mazet, R., Taylor, C. T., and Bechtol, C. O.: Amputation surgery and prosthetic prescription, J. Bone & Joint Surg. 38A: 1185, 1956.
11. Riordan, D. C.: Congenital absence of the radius, J. Bone & Joint Surg. 37A:1129, 1955.
12. Steensma, J.: Training the juvenile amputee, Orthop. & Prosthet. Appl. J. 6:18, 1952.
13. Thomas, A., and Haddan, C. C.: Amputation Prosthesis, Philadelphia, Lippincott, 1945.
14. Waddell, J., *et al.:* Training child amputees, Crippled Child, October, 1951.

Prosthetica in Amputatos Juvenil

Summario in Interlingua

Le studio, equipation prosthetic, e trainamento de novanta-cinque juveniles con varie typos de amputation traumatic e congenite ha revelate plure definite factos.

1. Le equipation prosthetic de juveniles pote esser interprendite con bon successo a un etate multo plus precoce que lo que es generalmente credite. Le manovra pote esser executate ante le etate de un anno.

2. Le effectos psychologic del amputation super tanto le patiente como etiam le parentes es multo plus considerabile que lo que ha essite comprendite in le passato. Le parentes e le juvene patiente deberea esser preparate psychologicamente pro le prothese.

3. Un programma de inseniamento in le melior uso del apparato prosthetic es indispensabile. Isto include regular visitas consecutori pro assecurar le correcte adjustamento, uso, e conforto del prosthese.

4. Un attitude conservatori verso methodos chirurgic es recommendate urgentemente. Centros de crescentia debe esser preservate, si del toto possibile, e omne le longor possibile debe esser preservate.

5. Le melior resultatos es obtenite per cooperative effortios prosthetic.

6. Copias, a dimensiones reducite, de apparatos prosthetic usate per adultos non es integremente satisfactori in le caso de patientes juvenil. Apparatos special es requirite.

18

Skin Grafts in Hand Surgery*

H. KELIKIAN, M.D., AND ARA DOUMANIAN, M.D.

Restorative surgery on crippled hands often necessitates simultaneous or preliminary skin grafting. Sometimes transference of skin from a distant source may be obviated by local shift: bones that cannot be put to any use are resected, and the skin thus made available is utilized to cover regional defects. In most instances it becomes expedient to supply the hand with skin from elsewhere—from a distant area.

FREE GRAFTS

Split-thickness free skin grafts are invaluable as temporary dressings for fresh or surgically revised wounds. Thicker free grafts can be used as permanent coverings for deeper defects of such areas as the palm, the digital pads, parieties of the fingers and even the dorsum of the hand. It is not advisable to apply free grafts on exposed tendons, nerves and blood vessels, but it sometimes becomes expedient to do so as a temporary measure. Free grafts are also used for covering defects left in the donor area after lifting a pedicled flap or tube. Sometimes the undersurface of the pedicled flap is lined with split-thickness skin graft, which is peeled off later—just before the denuded surface of the flap is applied to the defect on the hand.

The technic of transferring free grafts has been perfected to the extent of being mechanized. However, the general principles underlying the elevation and the shifting of pedicled skin are understood but vaguely.

ATTACHED GRAFTS

In reconstructive surgery on deformed hands we favor pedicled grafts for the simple reason that they are more likely to survive, and they convey an areolar seam which permits the tendons to glide and the joints to move. In children, when we cover the hands with transferred skin, we have to make allowance for growth, and pedicled grafts provide more extensible skin than free grafts, which tend to scar and bind, especially when they are thin.

VARIETIES OF ATTACHED GRAFTS

There are 2 main types of pedicled grafts: *tubes* and *flaps*. On its undersurface a flap may or may not be lined by split-thickness skin, while a tube is closed on itself by suturing together the cut edges so as to hide its areolar interior. A small circular or oval segment of an uncovered flap is called *petal-flap*, and when it has a short tube for a stalk it is named *stemmed-petal* (Fig. 1).

The general principles involved in raising various types of attached grafts are the same. Somewhat detailed descriptions of the steps whereby each of them is lifted should not be amiss, but first a few remarks about their source of supply.

THE DONOR SITE

The abdomen constitutes the most convenient region for elevation of pedicled grafts to be attached to the hand. It is im-

* From the Department of Orthopedic Surgery, Northwestern University Medical School, Chicago Wesley Memorial Hospital, Cook County Hospital, Chicago, Ill.

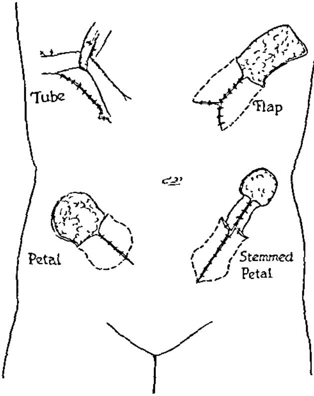


FIG. 1. Varieties of pedicled skin grafts lifted from the abdominal wall

portant that the area of the abdomen selected as the donor site be free of hair and it should bear a minimum amount of fat. A curious phenomenon, often noted in pedicled grafts transferred from the abdomen, is that in time they become pigmented, especially in brunettes, and they become fatter as the abdomen—to which they are no longer connected—becomes fatter. Disregarding this latent potentiality, preliminary to reconstructive surgery, we try to pile up on the hand more skin than we shall use, making allowance for wastage and future refinements After reconstructive work is completed, the graft on the hand may need "defattening" surgically; it may have to be revised and readjusted for a better cosmetic appearance.

In adults one can see which segment of the abdomen is hairy and which is hairless. In children we may have some difficulty in selecting an area that will not sprout hair at some future date. The sex of the child and its ancestry will provide clues. In general, hairy parents, especially those of

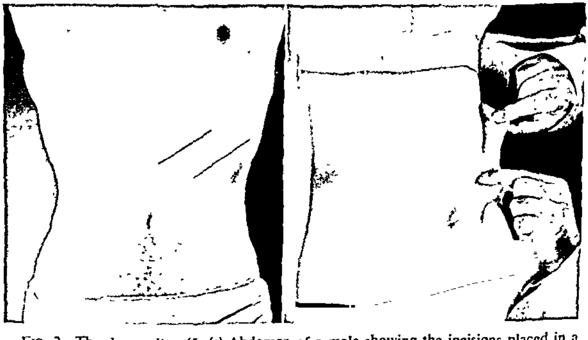


FIG. 2 The donor site. *(Left)* Abdomen of a male showing the incisions placed in a hairless area. Note the parallelogram pattern, which *proffers wider bases to penetrating* vessels than would have been possible had the incisions started and ended at the same *vertical lines (Right)* Abdomen *of a female showing the slant of the most easily* "pluckable" fold of skin Note the comparative paucity of hair in contrast with photograph at *left*

southern European and Mediterranean extraction, beget hairy offspring. In males, larger areas of the abdomen will be covered with hair than in females. In males one of the upper quadrants of the abdomen, the area over the lower ribs and the adjacent loin, constitute the best donor sites for elevation of pedicled grafts to be attached to the hand. In females, especially in blondes, the skin supplied by the lower abdomen and the contiguous loins will serve equally well. Needless to say, the pubic region should be avoided. For comfort and convenience, the side of the abdomen opposite to the hand to which the graft is to be attached is selected as the donor area.

When the mobility of the skin of the abdomen is tested, it will be found that the fold which is plucked most easily will slant from its lateral border down and medially —pointing to the umbilicus in the upper quadrant and to the pubis in the lower. The abdominal wall receives its nutrient supply from 2 main sets of vessels: epigastric and lateral segmental arteries. The superior and the inferior epigastric arteries pursue, more or less, an axial course and supply the middle segment of the abdominal wall. The segmental vessels—the lower intercostal and the lateral lumbar arteries—pierce the deep fascia along the outer border of the abdomen and run down and medially—parallel with the tension lines of the abdomen and in the same direction as the most easily "pluckable" fold of skin to be used for elevation of an attached graft. For better nourishment pedicled grafts must provide a wide base that falls in the path of these segmental vessels, and if the incisions are made parallel with the tension lines of the area more pliable skin will be obtained (Fig. 2).

Tube Grafts

For elevation of this variety of attached skin graft, 2 parallel incisions are made in the selected quadrant of the abdomen. The length of these incisions may vary from 2 to 5 inches, depending on the amount of skin needed; the interval between them should not be less than one third of their length. The closer "length to width ratio" approaches 2 to 1 the better. The incisions follow the direction of the tension lines of the abdomen; they start from the lateral border of either quadrant and run down and medially. The proximal incision starts at a point 1 or 2 inches medial to the inception of the distal incision and ends that much closer to the mid-line. If one visualizes imaginary lines connecting the beginnings and the ends of the 2 incisions, the result would be a parallelogram and not a rectangle, in which, everything being equal, the connecting lines are shorter. The parallelogram pattern provides a broader base to the outer pedicle of the graft and makes it available for a greater number of segmental vessels.

The skin incisions are developed down to the deep fascia—not through it—and the interval between them is cleared by blunt dissection. The skin between the 2 parallel incisions is undermined, and the flap thus procured is lifted and retracted by a tape. The skin edges on the donor site are undercut and released by small vertical slits which are placed at about ½ inch from where the skin edge of the donor area joins the cut margin of the lifted flap. The point made by the inner end of the proximal skin cut and its releasing slit is drawn under the bridge of the flap and is sutured to the apex of the angle produced by the 2 prongs of the corresponding releasing slit of the distal abdominal incision. This leaves a sharp corner between the stitch and the inner end of the distal abdominal incision. Medial to the stitch, the opposing skin cuts face each other in a zigzag fashion; they are approximated in such a way as to provide the adjacent pedicle the broadest base possible. A similar method is employed in closing the gap under the outer pedicle of the graft: here the point made by the releasing cut at the lateral end of the lower incision is sutured into the apex of the prong of the

corresponding slit of the upper leaf. The sharp corners at the outer angle of the proximal and the inner angle of the distal leaves are trimmed and rounded; the mobilized skin of the donor site is approximated under the bridge of the flap; the skin edges are sutured together by interrupted stainless steel wire. The cut margins of the flap are now defatted and sutured together, closing its areolar interior.

For attachment to the hand the pedicle nearer the mid-line is disconnected from the abdomen—usually 2 or 3 weeks later—by a half circular or an oval incision. The end petal of the skin thus raised should be about 1½ in. in diameter. The oval area of defect on the abdomen is closed by undermining the skin edges and drawing them together by interrupted wire sutures. Nearer the mid-line there will be some puckering which is done away with by running a small slit from the dome of the oval cut toward the mid-line and trimming the sharp corners thus created.

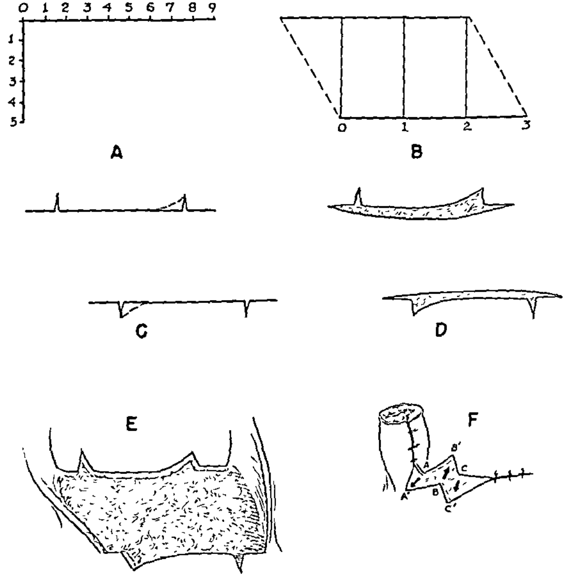


FIG 3 Illustrating some technical points in elevating a tube graft. (A) "Length to width ratio" of incisions; the interspace between them is shown here as being 9 to 5, almost 2 to 1. (B) Parallelogram pattern. (C) Relaxing slits and trimming sharp corners made by the main incisions and the small vertical cuts. (D) Undermining of the abdominal skin edges. (E) Denuded donor area after the intervening skin had been lifted. (F) Approximation of the skin edges near the base of the lifted tube.

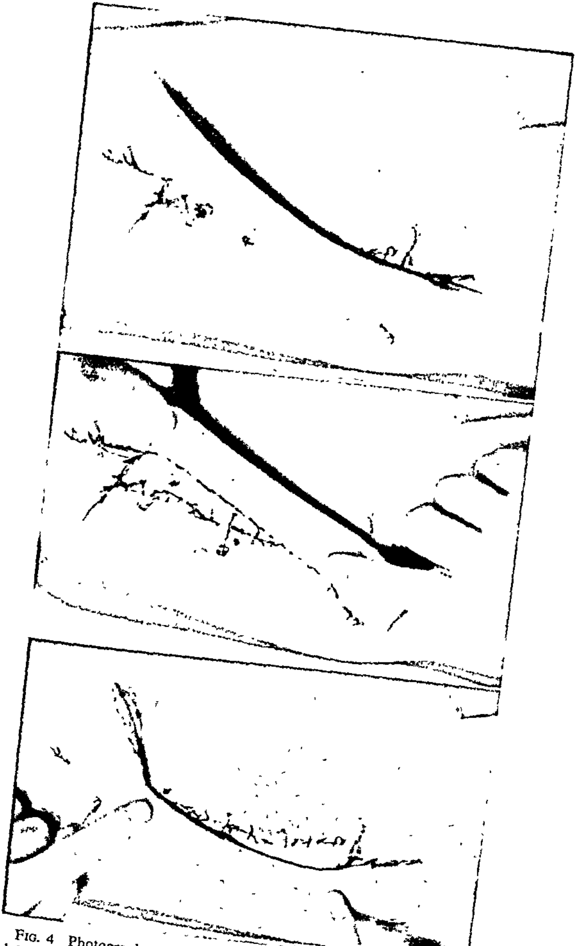


FIG. 4 Photographs of the lifted tube. *(Top)* Tube as it rests on the abdomen *(Center)* The same retracted to show the closure of the donor area near the inner pedicle of the tube. *(Bottom)* Closure at the outer pedicle of the tube

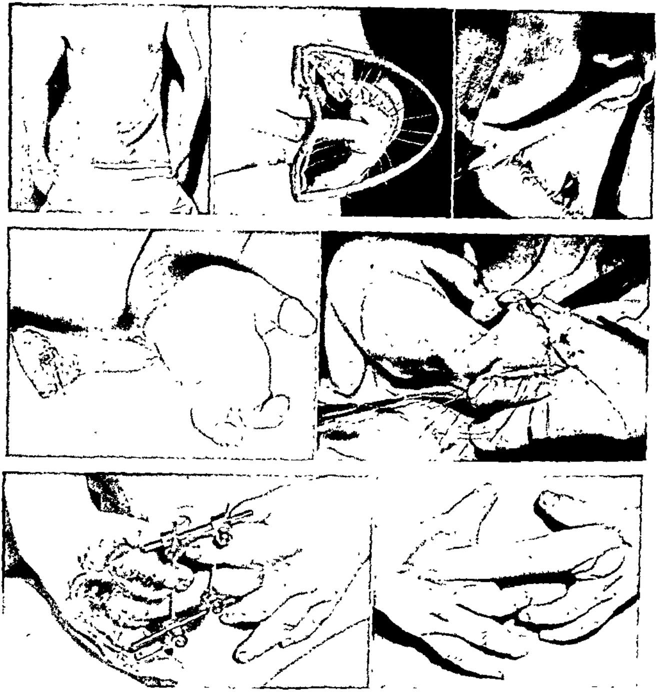


FIG. 5. Showing the transfer of the tube from abdomen to hand and from one hand to another hand. *(Top, left)* Tube with incisions healed. *(Top, center)* The inner pedicle of the tube has been freshly sutured to one of the web spaces of the hand. Wire sutures are twisted and tied over a catheter so as not to curl back and stick the patient. The arrangement keeps the wound dry and obviates accumulation of moisture and maceration. *(Top, right)* Tube attached to the hand firmly enough to permit stretching.

(Center, left) Here the nourishing pedicle has been weaned from the abdomen, and its end petal is closed on itself because of precarious circulation—before the tube is connected to the other part of the same limb or to the opposite hand. *(Center, right)* Tube freshly sutured from one hand to another.

(Bottom, left) A method of immobilization of attached hand. Note the Kirschner wires passing through two fingers—each belonging to one hand—and the connection to external bars for purposes of immobilization. *(Bottom, right)* Healed tube attached to both hands—before it is divided and portioned between the two hands.

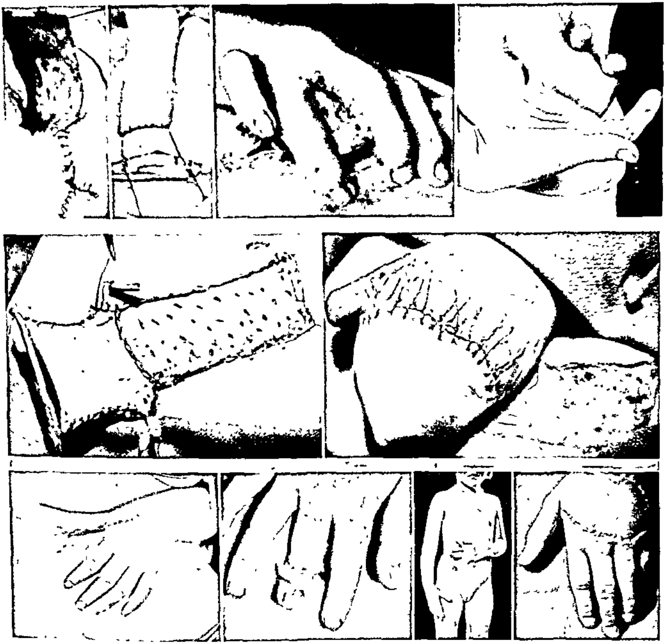


FIG. 6. Showing elevation of flaps and their transference to the hand. *(Top)* (A) Freshly lifted flap. Here the undersurface of the flap is lined with split-thickness skin. (B) Same with a "hook and eye" fixation over a pressure pad. (C) The flap has been hinged on its pedicle; split-thickness graft has been stripped from its undersurface, and the denuded strips of the flap are sutured to the volar surface of the fingers. (D) Same viewed from the volar aspect; note the Kirschner wire holding the two fingers separated. This is another way of applying a spreader splint.

(Center, left) A flap folded on itself to cover its areolar interior; the donor area has been lined with free skin graft. *(Center, right)* Degloved hand is pocketed between the folds of the graft shown at *left*.

(Bottom) (A) Flap sutured over the defect created by the ablation of the thumb. (B) Bipedicled flap slung across the denuded area over the extensor surface of the middle finger. (C) Tube converted to a bipedicled flap and bridged over the wound on the dorsum of the hand. (D) Flap transferred to the dorsum of the hand.



Fig. 7. Showing the elevation of the petal flap. *(Left)* Incision on the donor site. *(Center)* Trimming of the dog-ears. *(Right)* Lifted petal and closure of the defect on the donor area.

Tube is a valuable graft when a great amount of skin is needed for reconstructive work, especially when both hands are involved. About 7 weeks after connecting the end petal of the tube to one hand, the nourishing pedicle of the tube is weaned from the abdomen and attached to the other hand. After another 7 weeks the tube is divided in the middle and portioned between the 2 hands. At the time of weaning the tube from the abdomen, if its circulation appears precarious the end petal may be closed on itself or lined with split-thickness graft. Avascular skin will turn purplish or black in a week; then the end of the tube is trimmed down to a bleeding edge and is attached to another part of the same limb or to the opposite hand (Figs. 3, 4 & 5).



Fig. 8 Petal flap connected to the hand. *(Left)* Small petal flap sutured to the stump of an amputated index finger. *(Right)* Larger flap sutured to the surgically deepened web space between the index finger and the long finger in preparation for shifting the former radialward to take the place of the missing thumb

Tubes provide thick, unwieldy skin. When thinner skin is needed, as over the fingers and the dorsum of the hand, especially when one hand is involved, flaps are to be preferred. Incisions on the donor site for the outlining of a flap follow about the same general plan as those of the tube: they start from the lateral border of the abdomen and run down and medially, following the general direction of the tension lines of the region. The proximal incision starts at a

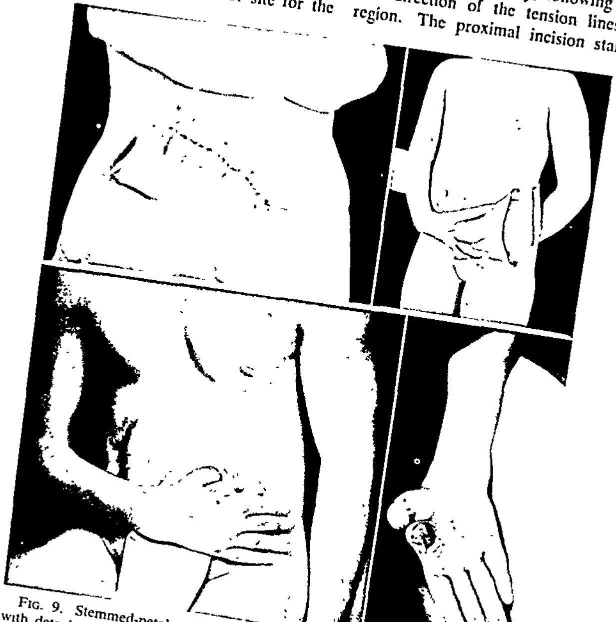


FIG. 9. Stemmed-petal types of pedicled graft. *(Top, left)* Stemmed petal with detached end closed on itself to see how much skin will slough and how much will survive *(Top, right)* Stemmed petal connected to the surgically deepened web space between the index finger and the long finger in the process of transferring the former to take the place of a missing thumb. Note the spreader splint, which consists of a catheter sutured to the fingernails and given firmness by a Kirschner wire. The spreader splint is connected to a bandage which is to go around the arm and the torso. *(Bottom, left)* Showing a short first metacarpal wrapped with available skin from the web between the thumb and the index ("phalangization" of the first metacarpal); the defect of the web space and the radial side of the second metacarpal is covered by the abdominal graft. *(Bottom, right)* Stemmed petal weaned through its tubular stalk.

point somewhat medial to the inception of the distal incision giving the pedicle of the flap wider base; the inner ends of the incisions may stop at the same vertical line. If the flap is too long, or very narrow, it is best to leave both pedicles attached for a few weeks. In single-pedicled flaps the inner ends of the incisions are joined, and the skin outlined is undermined, lifted and hinged laterally on its pedicle. The defect of the donor area is closed by undermining and releasing the proximal and the distal skin edges and approximating them. When the defect in the donor site is too wide, the skin edges are transfixed—sometimes partly approximated — by subcutaneous sutures, and the uncovered area is lined with split-thickness graft. The latter may be reflected to cover the undersurface of the flap. A pressure pad is applied on the donor area, and the flap is turned back over this and anchored by sutures or by a "hook and eye" arrangement at each of its free corners. Sometimes the flap is folded on itself in the manner of a pillowcase. When there is good healing and the wound is dry, the split-

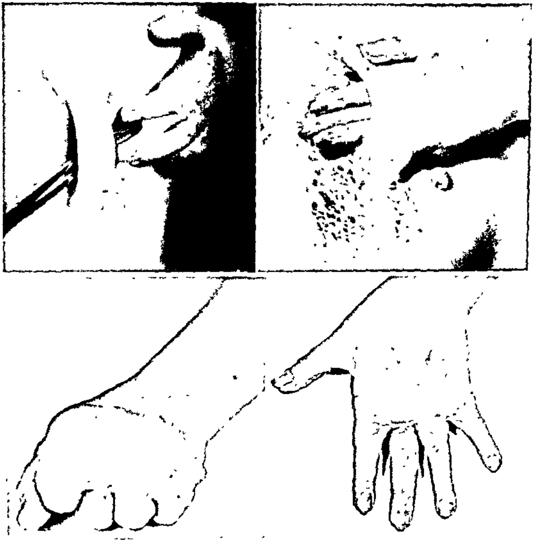


FIG 10 Replacement of a dorsal scar. Cicatrix over the dorsum of the hand due to an old burn; the extensor tendons of the three ulnar fingers were bound to the scar and would not permit closure of the hand into a fist. *(Top, left)* Showing the scarred hand and the abdominal tube under which the hand is to be tunneled *(Top, right)* The tube has been converted to a bipedicled flap and sutured to the denuded area left after dissection of the scarred skin. *(Bottom, left & right)* Functional results.



FIG. 11. Replacement of volar scar with contracture of three middle fingers. *(Left)* The hand before surgery. *(Center)* The same hand 7 weeks after excision of scar and covering the surgical defect with one end of the pedicled graft. In this picture the nourishing pedicle of the graft is shown weaned from the abdomen. Part of this tube was used to line the defect created by the extirpation of the scarred skin of the palm. *(Right)* The end-result.

thickness seam is peeled from the undersurface of the flap, and the denuded end-petal is used to cover the defect on the hand. In fresh or surgical wounds the uncovered undersurface of the flap can be applied directly to the wound on the hand (Fig. 6)

Petal-flap. The simple petal type of pedicled graft is fashioned by a semicircular incision, the apex of which points toward the mid-line of the abdomen. The petal is lifted in a plane superficial to the deep fascia and turned laterally on its pedicle. A small incision is made from the mid-point of its convex dome; the dog-ears thus produced are trimmed off, and the edges of the skin on the donor site are approximated by wire. Petal-flaps are especially useful when small areas need to be covered, as the tip of a finger or the webspace (Figs. 7 & 8).

Stemmed-petal. This is a petal-flap with a short segment of a tube as its stalk. For the preparation of a stemmed-petal, 2 parallel incisions 3 in. long are made over the abdomen; the interval between the 2 incisions should measure more than one third of their length. As in the case of tube grafts, the upper incisions start nearer the mid-line than the lower. Near the mid-line, the tips of the incisions are joined by a curved cut, and the flap is lifted in a plane superficial to the deep fascia. The skin edges of the donor area and at the neck of the graft are sewed together, leaving a circular petal for covering the defect on the hand—surgical or otherwise. When the stem of the graft is long it is wise to postpone the attachment of the graft to the hand and close the petal on itself to see how much of the tip will slough (Fig. 9).

PRACTICAL APPLICATIONS

Not all measures directed toward functional restoration of the damaged or the defective hand necessitate skin grafting. Many do. In some instances all that is needed is adequate skin covering or replacement of scars by pliable integument; in others skin grafting must be co-ordinated with other reconstructive measures. We shall confine our discussion to those conditions where skin grafting is paramount, if not the sole procedure.

Deep-seated Cicatrix Due to Burn

In the process of healing of third-degree



FIG. 12. Traumatic amputation of the distal phalanx through the matrix of the nail. *(Top, left)* Showing the gangrenous tip of the middle finger. This portion of the finger had been chopped off by a kitchen knife. It fell off and was picked from the floor and taken to the family physician, who sutured it back in place. *(Top, center)* The gangrenous fingertip, with a fragment of necrotic bone, was removed; the nail matrix was curetted, and a petal flap was sutured to the tip of the finger. Note the spreader splint. *(Top, right)* Velpeau bandage starting from the spreader splint.

(Bottom) (A & B) The general course of the foundation of the Velpeau bandage. (C & D) Final results; note the deepened pigmentation of the grafted skin

thermal injuries, thick welts of scar tissue will settle on the dorsum of the hand and bind the extensor tendons restraining the flexion of the finger; on the volar aspect they will bowstring across the joints as unyielding cords and prevent extension. In both instances contracted skin and underlying scar tissue must be dissected and replaced by areolar tissue-bearing skin which will allow the tendons to glide under and the joints to permit full motion (Figs. 10 & 11).

Traumatic Amputation of the Distal Phalanx Through the Matrix of the Nail

This injury is seen often in ? and housewives incident to chop ith a hatchet. Laboring men u e-

signed to having the remainder of the phalanx whittled away; then the wound may be closed with the skin thus made available. It is to be remembered that the base of the distal phalanx gives insertion to the long extensor and the deep flexor tendons, and it should be preserved. If the phalanx is amputated near its base the unsupported nail will keep growing and curl over the end of the finger. The nail and its matrix should be removed thoroughly prior to the closure of the stump by regional or by grafted integument. The germinal cells covered with skin will keep on proliferating and cause focal abs es (Fig. 12).

C ractures Where the s Are Exposed

In trial injuries where there

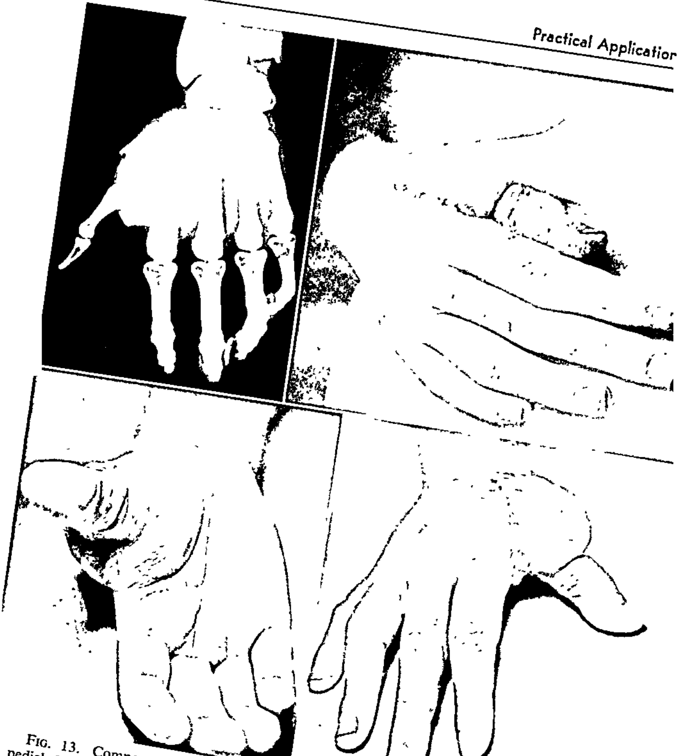


FIG. 13. Compound fracture of the thumb where exposed bone is covered with pedicled graft. *(Top, left)* Roentgenogram of the hand. *(Top, right)* Pedicled graft attached to the hand. Note that the stem of the pedicle and the index finger serve as side splints for the fractured metacarpal. *(Bottom, left)* Same, after weaning the skin graft, volar view of the hand. *(Bottom, right)* Dorsal view of the same; note the increased obesity of the graft.

is a large gaping wound over the hand and the fractured fragments of bone are visible or protrude, timely covering of the area will go a long way in obviating sepsis and loss of substance. The alignment of the broken bone is not as important and it can even be disregarded. When the fracture involves the metacarpal of the thumb, the pedicle of the skin graft on the one side and the index finger on the other will splint the broken



FIG. 12. Traumatic amputation of the distal phalanx through the matrix of the nail. *(Top, left)* Showing the gangrenous tip of the middle finger. This portion of the finger had been chopped off by a kitchen knife. It fell off and was picked from the floor and taken to the family physician, who sutured it back in place. *(Top, center)* The gangrenous fingertip, with a fragment of necrotic bone, was removed; the nail matrix was curetted, and a petal flap was sutured to the tip of the finger. Note the spreader splint. *(Top, right)* Velpeau bandage starting from the spreader splint.

(Bottom) (A & B) The general course of the foundation of the Velpeau bandage. (C & D) Final results; note the deepened pigmentation of the grafted skin.

thermal injuries, thick welts of scar tissue will settle on the dorsum of the hand and bind the extensor tendons restraining the flexion of the finger; on the volar aspect they will bowstring across the joints as unyielding cords and prevent extension. In both instances contracted skin and underlying scar tissue must be dissected and replaced by areolar tissue-bearing skin which will allow the tendons to glide under and the joints to permit full motion (Figs. 10 & 11).

Traumatic Amputation of the Distal Phalanx Through the Matrix of the Nail

This injury is seen often in butchers and housewives incident to chopping meat with a hatchet. Laboring men usually are resigned to having the remainder of the phalanx whittled away; then the wound may be closed with the skin thus made available. It is to be remembered that the base of the distal phalanx gives insertion to the long extensor and the deep flexor tendons, and it should be preserved If the phalanx is amputated near its base the unsupported nail will keep growing and curl over the end of the finger. The nail and its matrix should be removed thoroughly prior to the closure of the stump by regional or by grafted integument. The germinal cells covered with skin will keep on proliferating and cause focal abscesses (Fig. 12).

Compound Fractures Where the Bones Are Exposed

In war or industrial injuries where there

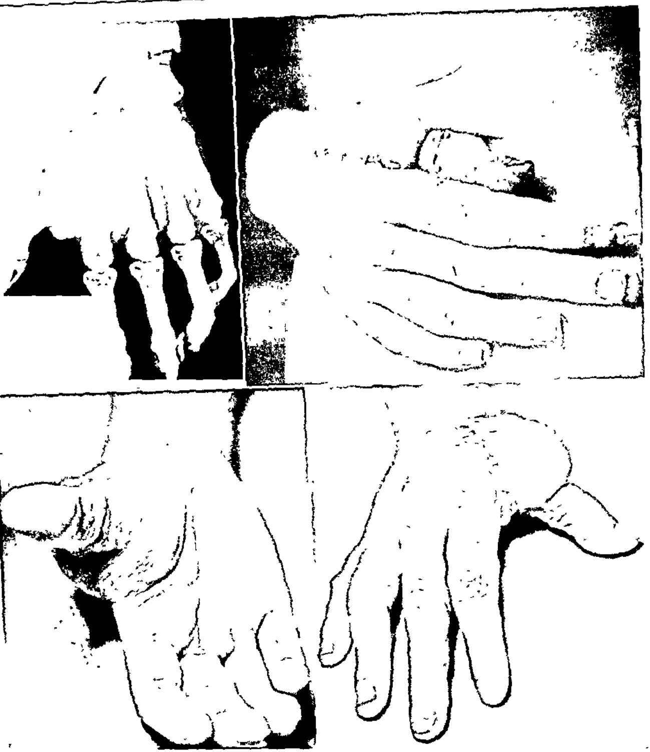


Fig. 13. Compound fracture of the thumb where exposed bone is covered with pedicled graft. (Top, left) Roentgenogram of the hand. *(Top, right)* Pedicled graft attached to the hand. Note that the stem of the pedicle and the index finger serve as side splints for the fractured metacarpal. *(Bottom, left)* Same, after weaning the skin graft; volar view of the hand. *(Bottom, right)* Dorsal view of the same; note the increased obesity of the graft.

is a large gaping wound over the hand and the fractured fragments of bone are visible or protrude, timely covering of the area will go a long way in obviating sepsis and loss of substance. The alignment of the broken bone is not as important and it can even be disregarded. When the fracture involves the metacarpal of the thumb, the pedicle of the skin graft on the one side and the index finger on the other will splint the broken



FIG. 14. Crushed hand with comminuted fractures of the phalanges and laceration of second, third and fourth fingers. The hand got caught between two iron railings, each weighing about 300 pounds. *(Top, left)* The hand 2 hours after the injury. *(Top, center)* Same hand after revision of the wounds. Devitalization was more extensive than was apparent. *(Top, right)* Covering the denuded areas with free grafts, the hand was splinted. *(Bottom, left)* The same 3 weeks later. *(Bottom, center)* small pedicled graft that was lifted from the abdomen at the time of primary surgery. *(Bottom, right)* Pedicled graft attached to the long finger which had lost its volar skin down to the tendon sheath.



bone. In fractures of the other fingers, especially when comminuted, connection of the pedicled graft to the hand causes considerable pain and inconvenience and should be postponed until the broken bones consolidate (Fig. 13).

Crushed Fingers Seen Soon After Injury

It is important to remember that crushed skin dies more extensively than will be apparent immediately after the injury. When a hand is seen soon after a compression injury—such as having been caught between 2 railings—our primary concern should be to remove all of the devitalized skin and subcutaneous tissue down to bleeding points. In revision of wounds, the nerves, the blood vessels, the tendons and the bones must be preserved if possible. Then full-thickness free skin graft is used as permanent covering for the more superficial wounds, but where the tendons are visible a pedicled graft is preferred. When there are associated fractures of the metacarpals or the phalanges and connection of the hand to the abdominal graft causes considerable pain and inconvenience, it might be expedient to cover the exposed tendon or its sheath with a temporary split-thickness graft and splint the hand. At the same time, a pedicled graft may be lifted from the abdomen with the idea that after the fractures have become consolidated the intermediary split-thickness



FIG. 15. Mangled and degloved hands. *(Top, left)* Photograph of the hand and the forearm a week after crushing of the hand by the rebound of an uncontrolled propeller of a boat. Primary treatment had been given elsewhere. We could not ascertain what had been done; the incision over the radial artery would make one suspect that this vessel was ligated. *(Top, center)* Volar view of the hand. *(Top, right)* Dorsal view of the hand. *(Bottom, left & right)* Volar and dorsal views of another degloved hand 6 days after the injury. The primary treatment had been given elsewhere.

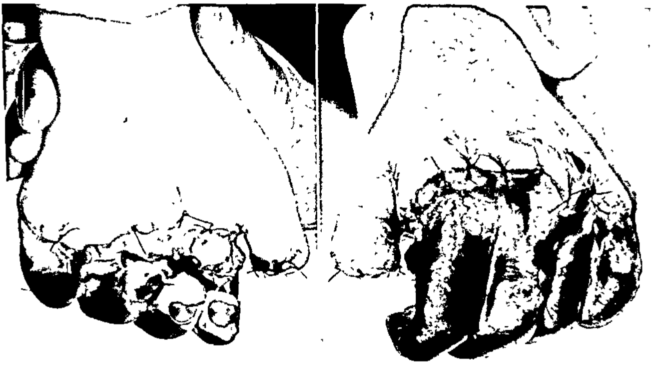




FIG. 16. The management of a degloved hand after the avulsed skin had been sutured back. *(Top, left)* Volar view of the hand when we first saw the patient. *(Top, center)* Profile view of the hand. *(Top, right)* The dorsal aspect. *(Bottom, left)* The same hand after gangrenous portions were removed. *(Bottom, center)* Abdominal flap folded on itself simulating a pillow case; note that the defect in the donor area has been covered with free graft. *(Bottom, right)* Denuded portions of the degloved hand were pocketed between the folds of the flap. *(Continued on next page)*



graft will be removed and replaced with areolar tissue-bearing integument (Fig. 14).

SEVERELY MANGLED AND DEGLOVED HAND

Crushed skin dies faster than the underlying tendons and bones. In severely crushed hands one should not underestimate the extent of devitalization and suture thick, dead skin over partly damaged, but as yet alive, structures such as the bones and the tendons. Equally erroneous, and tragic in consequence, is to lay back the skin that has been avulsed from the palm down to the fingertips. All that this accomplishes is to provide the injured fingers with a tight unyielding encasement, causing secondary compression and thrombosis of the vessels and inevitable necrosis of the tendons and bones which otherwise might have survived. A safe procedure is to remove all the devitalized skin, cover the hand with intermediary split-thickness graft and raise a pedicled graft from the abdomen for future use. When a degloved hand is seen after primary closure has been performed elsewhere, the best one can do is undo what



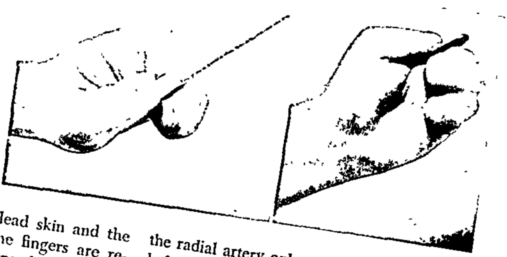


FIG. 16 *(Cont.)*. Functional results as enacted by the salvaged digits.

has been done: all the dead skin and the devitalized portions of the fingers are removed, and a pillowcase type abdominal flap is prepared. At a later date, the denuded portion of the hand is pocketed between the folds of the graft. Later on, the remnants of the fingers are separated and wrapped around with skin (Figs. 15 & 16).

Skin Graft To Improve the Circulation of Mummified Thumb and Permit Correction of Malposition by Osteotomy

The thumb has a unique and, at times, precarious circulation. Most of the common digital arteries supplying the other fingers branch out from the superficial palmar arch —the continuation of the ulnar artery—but receive sizable anastomotic twigs from the deep palmar arch, which is the continuation of the radial artery. The digital artery going to the volar aspect of the thumb comes from the radial artery only—from the main trunk before it becomes the deep palmar arch or from the arch itself. In injuries to the radial artery at the wrist, the tip of the thumb will slough, and the pollex as a whole will become mummified. A stiff thumb can still be of some use if it is not curled into the palm in the way of the other fingers. From the latter position the thumb can be brought into appositional position by osteotomy, but first the scarred skin at the base of the thumb must first be replaced by pliable integument. Replacement of adherent constricting scar by movable skin will enhance the circulation of the digit and promote healing of indolent wounds distally (Fig. 17).

Skin Grafts in Congenital Anomalies of the Hand

If restorative surgery is contemplated on the hands of a child born with confluence, absence or malformation of a finger, it

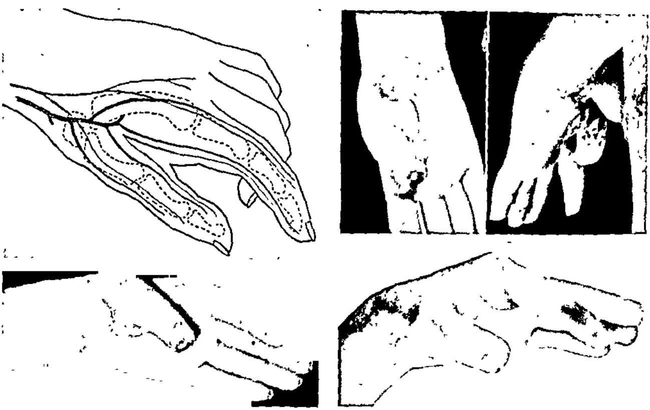


FIG. 17. Malpositioned, mummified thumb with gangrene of its tip due to injury to the radial artery at the wrist. *(Top, left)* Diagram showing the radial artery and its branches to the thumb. The thumb does not receive any tributaries from the ulnar artery or its continuation, the superficial palmar arch. *(Bottom, left)* The hand when first seen by us. *(Top, center)* Same hand, frontal view, showing the scar at the base of the thumb and the indolent ulcer at its tip. *(Top, right)* The scar tissue was replaced by a pedicled graft, which is shown here still connected to the abdomen. *(Bottom, right)* Final result. After replacement of scar tissue at the base of the thumb with pliable skin, a corrective osteotomy was done through the metacarpal bone. Note that the ulcer at the termination of the thumb has healed.

should be performed as early as possible—even in infancy. We quote from our article on this subject:

> Functional use is the greatest stimulus to growth and muscular co-ordination: fingers will grow and learn to work if they are freed from restraint and put in position for work.

In a considerable number of congenitally malformed hands skin grafting is a subsidiary link in the chain of procedures purporting to restore to the maimed limb a measure of usefulness and an appearance which is not, to say the least, unsightly. In some congenital anomalies, expeditious skin grafting makes more complicated operations on the bones and joints unnecessary.

Syndactylism provides a pertinent example. It matters little whether the adjacent parietes of the separated digits are covered with full-thickness free skin and the webspace between them is lined with a locally fashioned flap or by a pedicled graft, but it does make a great difference as to how early in life the confluent digits are separated and insulated by pliable skin. Again we quote from our article on the subject:

> When two fingers remain connected for a protracted period, the joints lose their motility, in the affected cleft the interosseous and lumbrical muscles atrophy. (Fig. 18)

In children born with absent phalanges, the hand is attached to a pedicled graft, and sufficient skin is piled up on it to enable us to deepen the webspaces between the fingers and later to cover the sides and the dorsum of the separated metacarpals. Skin supplied

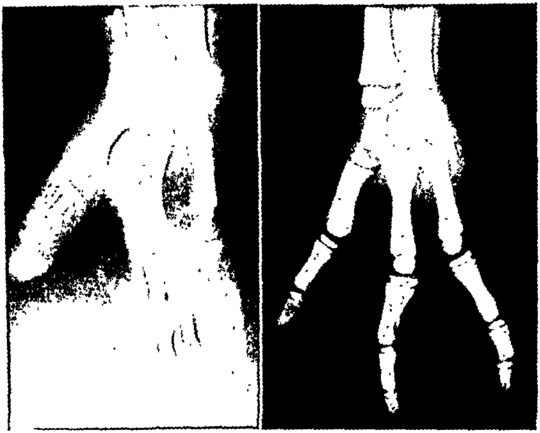
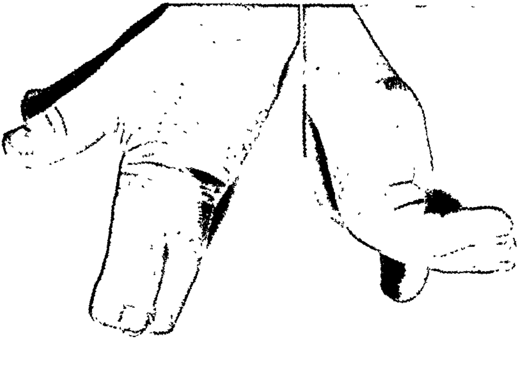


FIG. 18. Syndactylism treated with local readjustment of the available skin and pedicled skin graft in a boy about 5 years of age. *(Top, left)* Roentgenogram of the hand prior to surgery; note the delayed ossification of the carpal bones. *(Top, right)* Same hand 4 years after surgery; note the confluence of the carpal bones on the ulnar side of the wrist. This boy also had diastasis at the proximal radio-ulnar articulation. *(Bottom, left)* The hand before surgery. *(Bottom, right)* Showing the range of flexion of the confluent fingers. *(Continued on next page)*



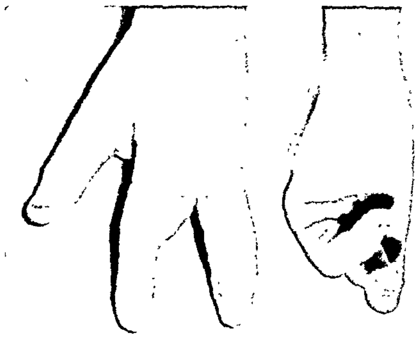


FIG. 18 *(Cont.)*. *(Left)* The distal portions of the digits were insulated with skin locally available; the phalanges seen at top, left, which had no supporting metacarpal bone, were removed; the adjacent bases of the two ulnar fingers and the web space between them were covered with a pedicled skin graft. *(Right)* Range of flexion 4 years later.

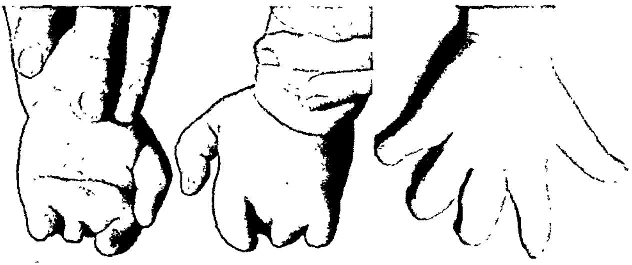
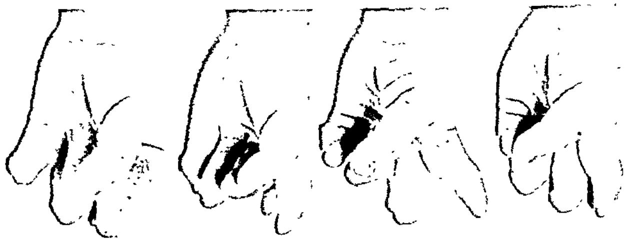


FIG. 19. Congenital absence of the phalanges of the four ulnar fingers treated by piling enough pedicled skin on the dorsum of the hand to enable us to deepen and cover the web spaces between the adactylic metacarpals. *(Top, left)* The hand before surgery. *(Top, right)* Palmar aspect of the same hand 3 years later. *(Bottom)* Functional results.



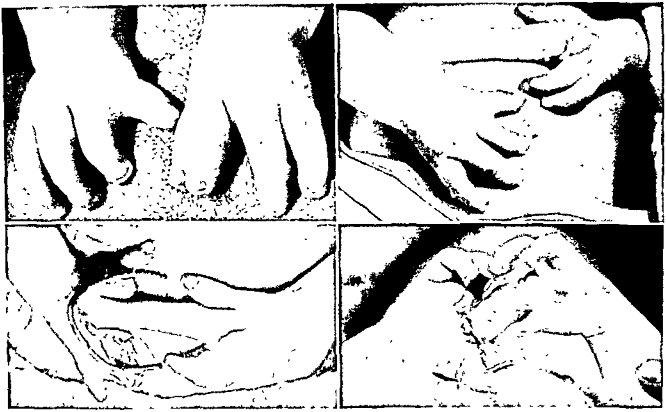
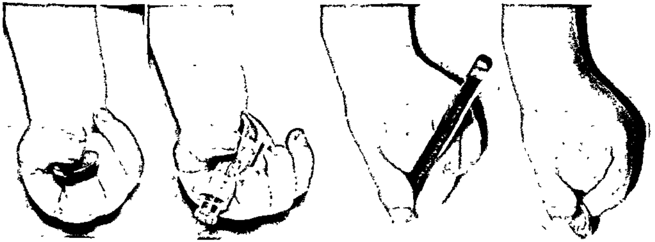


FIG. 20. Congenital absence of the thumbs in an infant 6 months old treated by deepening and widening the web spaces between the two radial fingers and lining the surgical cleft with skin supplied by a pedicled graft. *(Top, left)* The hand before surgery. The hand to the left had synostosis between the two radial metacarpals; these were separated by a chisel. The hand to the right had three phalanges in the ulnar finger of the syndactylized digits that had no supporting metacarpal; these phalanges were removed. *(Top, right)* Pedicled graft attached to the surgically deepened and widened web space of one hand. *(Center, left)* The other end of the graft freshly connected to the opposite hand. *(Center, right)* The undersurface of the same. *(Bottom, left)* The functional results of the hand with four fingers. *(Bottom, right)* The functional results of the hand with two fingers.



by a pedicled graft is not used to cover the tips or the palmar surfaces of the newly fashioned digits as they are devoid of sensations (Fig. 19).

In adults and older children, transference of the index finger to take the place of a missing thumb is an elaborate undertaking requiring as long as 6 or 7 months to finish,

several surgical sittings and many procedures: (1) deepening and widening of the webspace between the index finger and the long fingers; (2) lining the surgically deepened cleft by a pedicled skin graft; (3) later on, osteotomy of the index finger metacarpal and displacement of the distal fragment radialward and connecting it to the remnant of the first ray or to the greater multangular bone; (4) still later, osteotomy through the united metacarpal and gradual rotation of the index finger until it comes to face the other fingers; (5) sometimes delivery of the extensor tendon of the index finger from under the dorsal carpal ligament, shifting it toward the radial styloid and holding it there with a sling fashioned from part of the tendon of brachioradialis to make extensor serve as an abductor as well as extensor of the substituted pollex.

In infants all that is needed is to widen and deepen the webspace between the index finger and the long fingers, cover the surgical cleft with a pedicled graft and later locally tug and readjust the transferred skin until the index finger turns against the other fingers where it can function as a thumb—without displacement and rotary osteotomy of its metacarpal or extrication and transfer of its extensor tendon (Fig. 20).

BIBLIOGRAPHY

Kelikian, H , and Bintcliffe, E. W.: Functional restoration of the thumb, Surg , Gynec. & Obst. 83:807-814, 1946.

Kelikian, H., and Doumanian, A.: Congenital anomalies of the hand. In press.

Graffos Cutanee in Chirurgia del Mano

Summario in Interlingua

Chirurgia restaurative de manos mutilate require frequentemente transplantationes cutanee. Le technica del transferimento de graffos libere ha essite perfectionate a un grado que illo es un manovra routnari, sed il existe ancora un confusion considerabile relative al methodos del elevation e del transferimento de graffos pediculate.

Il existe quatro utile typos de graffo pediculate. Illos es (1) tubo, (2) panno, (3) petalo, e (4) petalo petiolate. Le abdomine es considerate como le plus commode sito donatori pro le elevation de graffos pediculate pro le mano. Le area contro-lateral del abdomine es seligite como sito donatori. Le area es disproviste de capillos. Le incisiones es placiate de maniera que le graffo ha le melior circulation possibile e possede un alte grado de elasticitate.

Pannos pediculate es usate pro restaurar profunde vulneres al asoecto dorsal e volar del mano. Illos es etiam usate pro coperir exponite tendones e nervos. Petalos o petalos a petiolo es utilissime pro coperir membranas interdigital post separation chirurgic interprendite in le essayo de mobilisar le ossos metacarpal o in preparation al transponimento del indice al loco del absente pollice. Digitos, specialmente le pollice, es a vices mumificate in consequentia de lesiones vascular. Nos utilisa transplantas cutanee pro reimplaciar integumento cicatrisate e executa le operation osteotomic plus tarde a transverso le pelle transplantate.

19

Total Excision of Semilunar Cartilages Through a Small Anterior Incision

DUNCAN C. MCKEEVER, M.D., F.A.C.S.*

In some orthopaedic clinics it is customary to remove only the anterior portion of the semilunar cartilage, but in a large series of cases it is necessary, at times, to remove the posterior portion later. Various abnormalities of traumatic origin may exist in the posterior part and make its removal mandatory. These are not always visible. Many experienced surgeons feel that total excision always should be done.

A wide variety of operative technics and special instruments have been recommended to facilitate total excision of the semilunar cartilages. Vertical incisions from 2 to 9 inches in length, dual anterior and posterior incisions and even transverse incision with severance or detachment of the collateral ligament have been recommended to obtain this objective.

The advantages of a small anterior incision are obvious They are: early ambulation, shorter hospitalization, easier rehabilitation and minimal permanent disability. Economic factors enhance the importance of all of these considerations.

The difficulty with an anterior incision has been that it seldom permitted complete excision of the cartilage. Numerous clamps and hooks, used to make traction on the cartilage during its excision, never were consistently successful. Special knives and cutting devices were either too cumbersome to use or they cut off the cartilage before reaching the posterior attachment. Many are dangerous, and serious accidents have occurred with some of them.

No claim to originality is made on the cartilage knives presented herewith (Fig. 1). When the author arrived at Navy Hospital No. 10 in January, 1944, 2 of these knives were among the orthopaedic instruments. Their exact origin is unknown to me although I have endeavored to ascertain it. Their purpose was readily apparent. They may be modified Breck knives.

The only change made in them has been the addition of the small beads at the tips of the V. This addition makes it somewhat easier to follow the marginal attachment of the cartilage and possibly may make the instrument safer, although no accidents occurred incident to the use of the original knives in over 200 cases. The technic was developed to utilize fully the advantages of the knives, and it has made total excision possible, through a small anterior incision, in almost 100 per cent of cases. The technic is as follows:

With the knee flexed over the end of the table, an incision about 1½ or 2 inches long is made over the anterior attachment of the cartilage at the level of the joint or crossing the joint. It may be oblique, vertical or transverse, as the operator wishes. The capsule may be opened in the same plane as the skin incision or in a different plane.

It is the author's custom to make an oblique or nearly transverse skin incision

* Houston, Tex.

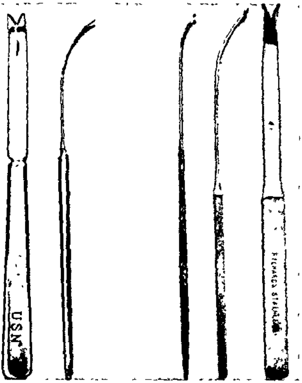


FIG. 1. *(Left)* Original knives. *(Right)* Modified knives.



FIG. 2. Severing antero-inferior edge of attachment.

and to incise the capsule almost vertically with the electric knife. Removal of the ligament of Wrisberg and a portion of the fat pad may be indicated, and this should be done with the electric knife for better hemostasis.

The secret of the success of the technic lies in the next step, which, for emphasis, is expressed in the following Latin phrase: *Facilium est extraheri retrorsum* ("It is easier to take it out backward"). We are accustomed to attack that portion of a problem that first makes its appearance in an incision. In this case the first thing we see is the anterior end of the semilunar cartilage, so we sever this attachment. Then follows the struggle to maintain some sort of grip on the cartilage while part or, if possible, all of the posterior portion is removed. This is difficult and at times impossible.

It is easier to take it out backward. A small incision is made along the anterior inferior edge of the attachment of the cartilage (Fig. 2). and a piece of gauze is passed through this incision and around the cartilage, leaving the anterior end of the cartilage

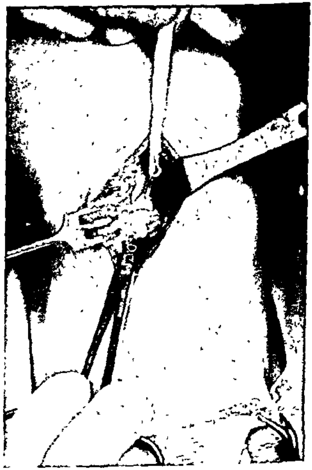


FIG. 3. Piece of gauze passed around cartilage for traction.



FIG. 7. Final step Severing anterior attachment.

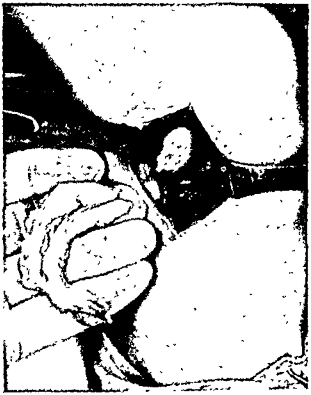


FIG 8. Total excision.



FIG. 9. Cartilages excised *in toto* by the technic described.

in some cases, where the joint is extremely loose, the entire cartilage may be removed with the scissors. However, after the anterior quadrant, or part of it, has been detached it is easier to insert the special knife, using one which best fits in the particular case. The knife with the greater curve usually fits best for cutting the posterior part of the marginal attachment. The knife edge should be held away from the cartilage, and the entire marginal attachment should be severed with a single cut, if possible, so that the beads will remain in proper relation to the cartilage (Fig. 4). After the marginal attachment is severed, continued pull on the gauze strip passing around the cartilage usually will displace it into the intercondylar notch (Fig. 5). Torsion on the lower leg to distract the joint surfaces may facilitate this. Using the knife with the smaller curve held with the blade flat and the curved end up, it is passed along the cartilage to the posterior attachment which then is severed under continued tension (Fig. 6). The cartilage flips forward out of the joint and remains attached only at the anterior end, which can be severed with a scalpel (Fig. 7). The cartilage is removed in toto, and the incision is closed (Fig. 8).

In cases where the cartilage is badly damaged, care must be used not to make too much traction because of the danger of pulling the cartilage in two during the process of its removal. It is also the author's custom to make an opening from the suprapatellar space into the area beneath the quadriceps muscle to permit any hemarrthrosis to escape.*

A pressure bandage is applied for 24 hours. Quadriceps setting exercises, which were started several days before the operation, are continued, and as soon as the patient is able to raise the extended leg off the bed he is permitted to walk without assistance of any kind. This is usually sometime between the second and the fifth days. Then the patient is permitted to leave the hospital. A simple cartilage excision case will be able to walk with a normal gait in 10 days or less, will be able to walk up and down steps in 1 to 2 weeks and should be able to return to office work or light work in 2 to 3 weeks and to heavy labor sometime between 3 and 6 weeks, depending on the individual.

If hemarthrosis develops it is aspirated, and a lytic enzyme is injected. Hydrocortone may be used if desired but it is rarely necessary.

SUMMARY

A technic to simplify total excision of semilunar cartilages through a small anterior incision is described. Knives designed to take advantage of the technic are presented (Fig. 9). Cartilages are removed by this technic.

* Chandler, Fremont A.: Closed drainage of the knee joint following arthrotomy, J. Bone & Joint Surg. 31A:580-581, 1949.

Excision Total de Cartilagines Semilunar a Transverso un Parve Incision Anterior

Summario in Interlingua

Le majoritate del experte chirurgos orthopedic recommenda excision total quando meniscectomia es indicate. Le previemente disponibile technicas de excision total requireva incisiones prolongate e a vices dual. Un parve incision anterior rende possibile le prompte restauration ambulatori, un breve periodo de hospitalisation, e le facile rehabilitation del patiente con minime grados de invaliditate permanente.

Le *majoritate del previemente elaborate* instrumentos pro le ablation de meniscos a transverso un parve incision anterior esseva inadequate. Certes esseva mesmo periculose. Cultellos in forma de 'V' (con non-acute perlas guidatori al punctas del 'V') ha essite *usate con bon successo pro excider* meniscos a transverso un parve incision anterior. Le technica usate es le sequente:

Le articulation es flectite a 90 grados, e un incision vertical, oblique, o transverse de un longor de 4 cm es facite supra le attachamento anterior del menisco. Es effectuate un parve incision que seque le margine anteroinferior del menisco e rende possibile le passage de un pecia de gaza circa le cartilagine. Traction es exercite per medio de iste gaza, resultante in un tendentia del menisco a displaciar se verso le incisura intercondylar. Per medio del cultello in forma de 'V,' le *attachamento peripheric es dissecate* in un sol tracto usque al attachamento posterior. In iste manovra un del perlas se move supra le menisco, le altere infra le menisco. Le mesme cultello, in un rotation de 90 grados, servi a separar le termino posterior del menisco ab su attachamento. Iste separation posterior rende possibile le ablation retrorse del cartilagine. Post que le attachamento posterior es separate, on separa le attachamento anterior e abfere le cartilagine. Le *secreto del successo de iste manovra jace in* le principio (hic formulate in latino pro render lo plus emphatic): *Facilium est extraheri retrorsum*, i.e., "il es plus facile extraher lo retrorsemente." Multo plus facile! Le ablation es plus complete, le rehabilitation es plus rapide, e le resultante invaliditate permanente es minimal.

20

Disability Following Crush Fracture of the Calcaneus

C. F. Ferciot, M.D.*

The severe disability that follows crushing fractures of the heel is a continuing challenge to the medical profession. A review of the literature clarifies the evolution of our present methods of management. At the turn of the century, treatment consisted of simple protection until healing had occurred, with return to functional activity as soon as possible. Later methods varied from gentle manipulation to more complicated procedures of reduction, some involving skeletal traction and forceful molding of the fragments. More recently, early open reduction of certain fractures has been done with bone grafting to replace the compressed cancellous bone and to restore contour and stability. In 1938, Goff published an excellent review of the literature and described a method of early manipulative reduction by means of a modified carpenter's clamp, followed by plaster fixation until healing occurred. Relatively early operative fusion of certain severely compromised joints has been advocated by various authors with encouraging results.

In 1935, Conn, reporting on a series of fresh fractures treated by early subtalar fusion, stated that "unsatisfactory feet" resulted in approximately one third of his cases On operative exposure of the subtalar joint, he was impressed by the extent of joint involvement found in contrast to the roentgenographic appearance of the bones. Suspecting that the same condition might exist in relation to the talonavicular joint, he began fusing this joint as well, and reported that "though the expected roughening and erosion of the joint was not often observed" he, nevertheless, felt that the end results following triple arthrodesis were superior to those that he obtained by simple subtalar fusion. On the basis of his experience, Conn voiced his firm conclusion that triple arthrodesis was the procedure of choice in the surgical management of severe crush fractures of the heel. This opinion has continued to influence orthopaedic thinking to the present time. In his hands I am certain that the results were excellent, but the fact remains that this method has not been adopted generally. Clinical observation disclosed that a triple arthrodesis leaves much to be desired from a functional standpoint, since it necessarily restricts mobility of the foot and makes walking on uneven surfaces difficult. Doubtless, this well-known and inevitable loss of mobility and function has been a deterrent to the more extensive use of this procedure as a primary treatment.

Palmer, in a paper published in 1948, clarified the mechanism of certain fractures of the heel and reported his experience with early operative reduction and bone grafting. Early anatomic and functional results appear to be very good, with all of the patients returning to work in an interval of 4 to 8

* The Lincoln Orthopedic and Rehabilitation Center, Lincoln, Neb.

TABLE 1. SUBTALAR JOINT INVOLVEMENT

Minimal	23	26.3%
Moderate	42	48.4%
Severe disruption	22	25.3%
	87	100.0%
Having associated fractures	11	12.6%

months after surgery. Some restriction of subtalar motion was present in most cases, but he reported that such motion was painless. It seems probable that this technic offers a decided improvement in the treatment of selected cases, particularly in the younger age group. It does require the exercise of an unusual degree of judgment and skill, and it seems certain that, were its use general, a considerable number of complications would eventuate. Further experience is necessary to evaluate properly its ultimate merit.

A series of 87 fractures of the os calcis seen in our clinic were reviewed, and it was found that over 97 per cent of these patients, regardless of their method of treatment or the severity of their injury, had returned to a good degree of functional activity in less than 2 years. In this entire group, 23 fractures were minimal, 42 fractures showed definite impaction with probable involvement of the subtalar joint and 22 cases were severe crush fractures with complete disruption of the subtalar joint Practically all of the second and third degree fractures healed with a marked reduction of subtalar motion, and several had a complete loss of this movement. The very satisfactory function observed in this latter group of patients where subtalar fusion developed spontaneously certainly indicates that a triple fusion operation is not necessary in every case of severe crush fracture.

TABLE 2. UNILATERAL CASES HAVING FUSION

	No. of Cases	Residual Disability
Triple arthrodesis	4	26%
Limited fusion	3	17%

A review of the group of 7 unilateral fractures having surgical treatment since 1951 showed that 3 of these patients had associated fractures of other bones. These patients all had involvement of the subtalar joint, and a triple arthrodesis was carried out in 4 cases, while a limited fusion procedure was done on the other 3. Five of these patients were treated for recent fracture, and 2 cases were treated for late disability. The average disability in the 3 cases having limited fusion was 17 per cent, while the disability of those having triple arthrodesis was 26 per cent. This 43 per cent higher disability rating is not particularly conclusive in a small series such as this, but I do feel that it is significant.

A group of 10 patients sustained bilateral fractures of the os calcis. Their average age was 53.6 years. In only 1 instance was the severity of fracture minimal. Only 3 of these patients had associated fractures of other bones, but 5 of them required surgical fusion. Of these 5 patients coming to surgical stabilization, 2 were treated primarily, 2 were referred to us late with residual disability and in 1 instance surgery was delayed because of severe associated injuries.

Cases 1 and 2 in this series illustrate the problem that arises in the management of severe bilateral crush fractures of the heel. The fractures were essentially symmetrical,

TABLE 3. CASES OF BILATERAL FRACTURE OF CALCANEUM

	Number of Cases
Minimal subtalar involvement	1
One minimal with the other moderate	2
Both moderate	2
Both severe disruption	5
Total	10
Feet having fusions	6 or 30%



FIG. 1. *(Top, left & center)* Showing severe bilateral crush fractures. *(Top, right)* Left foot after manipulation and early healing. *(Bottom, left & center)* Note calcaneocuboid involvement. This may result in persisting disability. *(Bottom, right)* Left foot after subtalar and calcaneocuboid bone-graft fusion.



and disruption of the subtalar joints was severe. These cases will be summarized briefly.

Case 1. A white male, aged 27 years, height 5 feet 7 inches, weight 190 pounds. This man fell 15 feet from a ladder on October 24, 1953, suffering bilateral severe crush fractures of the heel Manipulative reduction under spinal anesthesia was done within 3 hours and the position held in mild equinus by a snugly molded plaster cast. Casts were changed 10 days later and were removed at the end of 5½ weeks when roentgenograms showed satisfactory positioning but with marked involvement of the subtalar joint on both sides. Triple arthrodesis was done on the right foot on December 3, 1953, and plaster fixation continued for 8 weeks. The left foot

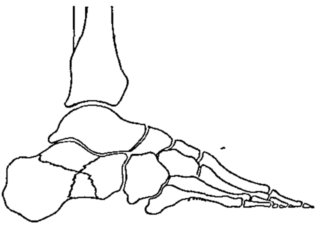


FIG. 2. Severe crush fracture after reduction and cast fixation for 5 weeks. General bony relationships have been restored, and healing is taking place.

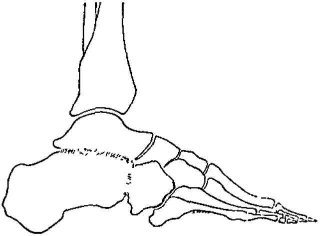


FIG. 3. Involved subtalar and calcaneocuboid joints have been stabilized, bone graft being used to maintain normal architecture of the foot. Surgery is easier at this stage due to decalcification of bone; healing progresses rapidly.

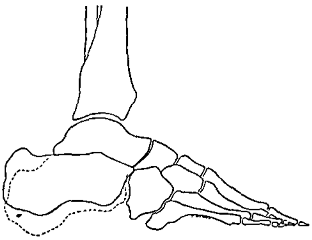


FIG. 4. Illustrating distortion of foot that may follow fusion by simple joint excision.

had a calcaneocuboid fusion on February 22, 1954, and the cast was continued for 6 weeks. The patient returned to work on May 18, 1954. A settlement of his compensation claim was made on June 16, 1954, with a disability rating of 18 per cent on the right foot and 15 per cent on the left foot. When contacted February 19, 1956, he reported that he had been working regularly as a truck driver and felt that the left foot was more functional because of its greater mobility.

Case 2. A white male, aged 49 years. This man suffered severe bilateral crush fractures of the heel on March 4, 1954, when he was thrown from an earth-moving vehicle. He had an associated minimal compression fracture of the body of L-1 and a Grade 1 spondylolisthesis at the lumbosacral level. He was admitted to the hospital 1 day after injury with marked swelling and was treated by elevation and compression until March 9, 1954, when manipulative reduction was carried out under spinal anesthesia, followed by fixation in molded plaster. The casts were removed after 4½ weeks, and roentgenograms showed disruption of the subtalar joint, but with good general bony relationships. A triple arthrodesis was done on the right foot on April 5, 1954, and cast fixation was continued for 10 weeks. Similar findings were present on the left foot, and a talocalcaneal fusion with bone grafting was done on this foot on April 29, 1954, and cast fixation was continued for 10 weeks. Considerable tenderness under the left heel persisted, and on April 7, 1955, the weight-bearing surface beneath the left heel was exposed surgically, and the irregular bone was smoothed. He returned to light work on August 15, 1955, and when last seen on February 13, 1956, he complained of some discomfort and tiring in the right foot after use. However, the triple fusion was firm and painless. Good mobility of the medial side of the left foot was evident, and the patient felt this to be his better foot.

In both of these patients it was obviously undesirable to do a triple arthrodesis on both feet, and for this reason a limited fusion was done on the second foot. The general architecture of the foot was first restored by a manipulative reduction, and, when early callus formation had occurred, the triple fusion was carried out on the right side. Later, a limited fusion was done on the left foot, utilizing iliac bone graft to stabilize the foot and to maintain anatomic relationships. In none of the patients so treated has there been evidence of progressive foot strain or degenerative change involving the talonavicular joint

Review of the functional relationships of the foot makes it evident that it is desirable to conserve the flexibility of the medial side of the foot, especially when subtalar motion is lost. The role of the peroneus longus muscle in holding the first metatarsal head downward in the standing or weight-bearing position becomes very important with loss of subastragalar motion, and any impairment of

its function leads to foot strain. The resultant symptoms often are mistaken for signs of talonavicular injury or strain. Immediate reduction of the fracture with careful molding of the bulging beneath the lateral malleolus will lessen the danger of adhesions to, and bony impingement upon, this tendon as it passes in close relationship to the talocalcaneal joint. It is probable that one of the most important accomplishments of open reduction stems from the free release of the peroneal tendons. Disruption of the calcaneocuboid joint must not be overlooked as it is often an unrecognized source of persistent disability.

In view of the very satisfactory results that have been reported by others who have utilized limited fusions and the good function that we have observed in our own cases, I am firmly convinced that fusion of the talonavicular joint should not be done unless the fracture involves this joint, or unless this step is necessary for the correction of faulty weight bearing position of the foot.

CONCLUSIONS

1. Severe crush fractures of the calcaneus should be treated by immediate reduction, utilizing spinal anesthesia or paravertebral block to improve the circulation and to lessen soft tissue swelling.

2. Reduction can be maintained by a snugly molded plaster dressing until callus formation becomes firm after 5 weeks, at which time the cast can be removed and the relationships of the calcaneal joints reevaluated.

3. Severely disrupted joints evident at this time should be treated in patients of all ages by early bone grafting fusion. This preserves the normal architectural relationships of the foot and favors an early return to functional activity.

4. A satisfactory degree of function usually follows adequate management.

BIBLIOGRAPHY

Barnard, L., and Odegard, J. K.: Conservative approach in the treatment of fractures of the calcaneus, J. Bone & Joint Surg. 37A:1231-1236, 1955.

Bohler, L.: Diagnosis, pathology, and treatment of fractures of the os calcis, J. Bone & Joint Surg. 29:75-89, 1931.

Conn, H. R.: The treatment of fractures of the os calcis, J. Bone & Joint Surg. 38:392-405, 1935.

Ferciot, C. F., and Stone, F. P.: Management of fractures of the os calcis, Nebraska M. J. 34: 55, 1949.

Goff, C. W.: Fresh fracture of the os calcis, Arch. Surg. 36:744-765, 1938.

McBride, Earl D.: Fractures of the calcaneum: tripod pin traction apparatus, J. Bone & Joint Surg. 26:578-579, 1944.

Palmer, I.: The mechanism and treatment of fractures of the calcaneus, J. Bone & Joint Surg. 30A:2-8, 1948.

Schofield, R. O.: Fractures of the os calcis, J. Bone & Joint Surg. 34:566-580, 1936.

Watson-Jones, R.: Fractures and Joint Injuries, ed. 4, Edinburgh, Livingstone, 1952.

Wilson, P. D.: Management of Fractures and Dislocations, Philadelphia, Lippincott, 1938.

Invaliditate post Fractura Comminutive del Calcaneo

Summario in Interlingua

Post presentar un revista del litteratura, le autor argue in favor del tractamento conservative de sever fracturas comminutive del calcaneo. Certe principios fundamental deberea esser observate:

1. Sever fracturas comminutive del calcaneo deberea esser tractate per reduction immediate. In isto anesthesia spinal o bloco para-vertebral deberea esser utilisate pro meliorar le circulation e reducer le intumescentia del histos molle.

2. Le reduction es a mantener per un ben adjustate application gypsate usque al prime formation callose post un periodo de circa

cinque septimanas. A iste tempore le relationes del articulationes calcanee es a re-evalutar.

3. A iste tempore, severmente disrumpite articulationes es a tractar per medio de un typo de fusion a graffo ossee que preserva le normal relationes architectural del pede e promove le retorno a activitates functional.

Le autor opina que arthrodese triplice es rarmente necessari e que solmente le disrumpite articulationes deberea esser stabilisate. Le articulation talo-navicular es rarmente implicate directemente e fusiones de iste articulation es rarmente necessari. Un revista de 87 casos indica que un grado satisfactori de function resulta de adequate formas de tractamento in plus que 95 pro cento del casos.

21

Avulsion of the Ischial Apophysis*

EDGAR A. ROGGE, M.D., AND ROBERT L. ROMANO, M.D.

Avulsion of the ischial apophysis is relatively infrequent; only a few cases have been reported in the medical literature. The first case was recorded in the American literature by Berry in 1912.[2] Since then, less than 2 dozen cases have been reported.

All of these cases are markedly similar in both their mechanism of production and in symptomatology; the syndrome is quite characteristic. They have occurred while the individual was engaged in strenuous activity such as playing football, running the high hurdle, acrobatic dancing or during any activity in which there is sudden extension of the knee with the thigh flexed, or sudden flexion of the thigh with the knee extended. In other words, the mechanism is that of sudden straight leg raising which snaps the hamstrings tight with consequent avulsion of their origin from the ischial tuberosity.

The age of fusion of the ischial apophysis is described as being between 18 to 25 years. The reported cases have been prior to the age of 25, most of them occurring between 14 and 24 years. Thus, the upper age limit corresponds closely with that of fusion of the apophysis. While McMaster[5] and Scott[8] raise the question of epiphysitis as an etiologic factor in this syndrome, Milch[7] and others believe that trauma, due to muscular violence, is the sole cause. In our experience of 2 cases, together with a review of the literature, we believe that trauma is the cause.

* From the Division of Orthopaedic Surgery, University of Washington School of Medicine, Seattle, Wash.

The usual situation occurs in an individual under 25 who forcibly stretches his hamstrings during a maximum effort. There is a sudden pain in the region of the buttocks with localized tenderness over the ischial tuberosity and pain on stretching the hamstrings. Following this, any activity, such as sitting, which puts tension on the hamstrings produces pain because of direct pressure on the ischial tuberosity.

The clinical course depends on the degree of separation. An avulsion of the ischial apophysis appears as an irregular crescentic shadow on roentgenographic examination. In one case there appeared to be some periosteal new bone formation. A tumor was considered by the roentgenologist. The fragment was excised, and the subsequent clinical course ruled out such a possibility.

If the fragment (the apophysis) is slightly separated, union will usually take place following rest. If there is a wider separation, healing by fibrous union may occur with a good clinical result assured. However, some cases apparently go on to nonunion with persisting pain In such instances excision of the fragment is probably the treatment of choice. One case demonstrates the chronicity or prolonged disability that may be encountered; this boy was unable to participate in sports for 3 years following his ischial apophyseal avulsion but became completely asymptomatic following excision of the nonunited fragment.

Two cases are presented, with the hope that interest may be stimulated in recognizing the entity more often.

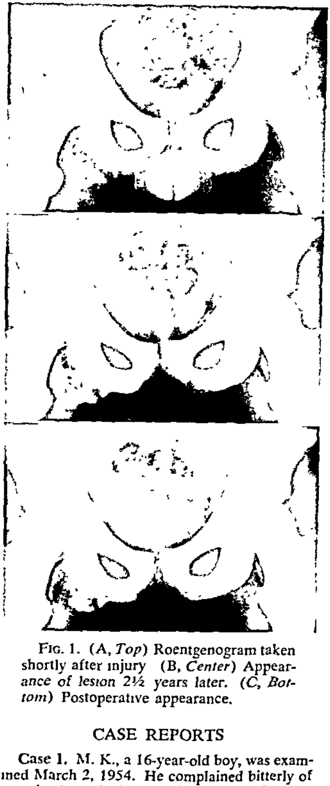


FIG. 1. (A, *Top*) Roentgenogram taken shortly after injury (B, *Center*) Appearance of lesion 2½ years later. (C, *Bottom*) Postoperative appearance.

CASE REPORTS

Case 1. M. K., a 16-year-old boy, was examined March 2, 1954. He complained bitterly of pain in the right hip that had become increasingly severe following an old football injury 3 years before The pain in his hip had become so severe that it was necessary for him to give up high school football. He was also unable to participate in baseball the following spring.

In 1951, this youngster was playing touch football and, after running 10 or 15 yards, he tripped on the turf His right leg "bent backward" as he fell, and a sudden severe pain was felt in the back side of his right hip. He was carried off the field. During the next 2 weeks he walked with the aid of crutches. He limped for several months. It was necessary for him to give up all sports for the next 1½ years. Roentgenograms of the pelvis taken shortly after the injury revealed the detached fragment of bone from the apophysis of the right ischium (Fig 1A).

He again participated in sports, but a recurrence of pain while playing baseball caused him to give it up.

This well-developed husky male, 5 feet 10 inches tall, weighing 175 pounds, appeared relatively normal; the only abnormal findings were confined to the region of his right hip. On deep palpation there was tenderness over the right gluteal fold. There was no restriction of hip motion. Straight leg raising was possible to 90°. Reflexes were normal. There were no inequalities of leg length, nor was there any evidence of atrophy. Roentgenograms of the pelvis taken at this time and compared with previous films showed that the detached fragment of the ischium was now approximately 2 inches in diameter and was separated from its intended attachment (Fig. 1 B and C).

Surgical exploration of this area was done 3 years after injury. A curved incision was made parallel to the gluteal crease. The detached fragment was revealed to be densely adherent to the tendinous origins of the hamstring muscles. Before the fragment was dissected and excised it was grasped with a towel clip to demonstrate its mobility. The postoperative course was uneventful. There was some muscle spasm and pain during the 4 days following surgery, but it was not considered necessary to immobilize the extremity. The specimen consisted of cortical and cancellous bone; no abnormalities were reported by the pathologist.

The patient was ambulatory without crutches 2 weeks after surgery and played high school baseball and football later the same year. The only residue following surgery has been a mild paresthesia, limited to the right thigh, believed to be due to compression of the posterior femoral cutaneous nerve. The skin sensation was otherwise normal. There were no abnormalities of the musculature. A normal range of motion of the hip and the knee followed recovery.

Case 2. D. R., a 15-year-old boy, sustained an injury while pole vaulting. He came down a distance of 9 feet, landed on his left leg, then fell over on his left side. This was followed by a dull, aching pain on the side of the left hip. This pain was constant and was especially aggra-

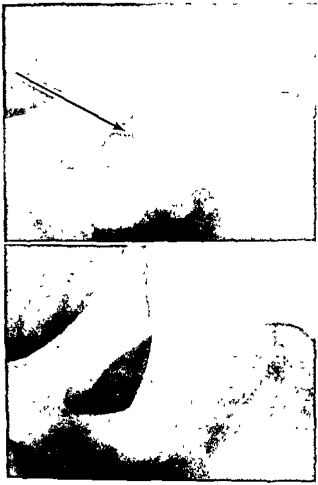


FIG. 2. (A, *Top*) Appearance of lesion 6 months after injury. Note elevation of the periosteum (arrow). (B, *Bottom*) Postoperative appearance.

vated by sitting and running. Sitting proved to be a handicap at school and also at home, where he was able to sit only long enough to have his meals, preferring at other times to lie on the floor.

He was a well-developed boy for his age of 15 years, 5 feet 10 inches tall, weighing 135 pounds. A general physical examination proved the patient to be normal, with the exception of a mild case of acne vulgaris. There were no painful areas except along the posterior aspect of the left hip, which was moderately tender on deep palpation. Motion of the hip joint was normal on both sides. Straight leg raising was possible to 85°. The patellar and the ankle tendon reflexes were normal. Leg lengths were equal, and there was no muscular atrophy or weakness. Roentgenograms showed an irregular shaving of bone from the tuberosity of the ischium on the left side (Fig 2 A and B). There existed also a curious elevation of the periosteum of the superior border of the inferior ramus of the ischium. Because of the irregular bone formation and a



FIG. 3. (A, *Top*) Appearance at operation, showing close relation of the femoral cutaneous nerve (dotted area) to the ischial tuberosity (i.t.). (B, *Bottom*) Cartilaginous fragments removed at operation.

superimposed shadow, the question of chondrosarcoma was raised.

This patient had been under a conservative regimen of treatment for 6 months, which included a month of bed rest, and was becoming very discouraged because of his prolonged inactivity. Blood sedimentation rate, alkaline phosphatase, acid phosphatase and urinalysis all

were normal. A surgical operation was done 8 months after the injury. This time a more extensive exposure was accomplished in order to visualize better the sciatic and the posterior femoral cutaneous nerves. This was accomplished by extending the curved incision, used in the first case, proximally to and along the greater trochanter and distally to the mid-line of the thigh. This incision permitted the gluteus maximus to be reflected, avoiding the posterior cutaneous nerve (Fig. 3 A).

The avulsed fragment was free, consisting of both bone and cartilage (Fig. 3 B). It was found to be incorporated firmly in the tendinous origin of the hamstring muscles, as in Case 1. Histologic sectioning revealed the specimen to be an epiphysis with evidence of growth, but not of neoplastic character.

The patient was able to leave the hospital a week after the operation and was ambulatory without crutches after another 10 days, remaining completely asymptomatic. He returned to competitive sports.

DISCUSSION

From the infrequency with which such a detached apophysis leads to surgical removal, it would appear that minor separations may require little or no treatment. Most of such avulsions will reunite, manifesting their disturbance at a later date only by chance when a roentgenogram may reveal a broadening of the lower ramus of the ischium. Only those individuals who have detached a substantially large fragment and are having symptoms should undergo operation.

In Case 1 the avulsed fragment probably healed by fibrous union so that the patient was asymptomatic when he first returned to sports 1½ years following his injury. He again experienced pain on resumption of vigorous muscular exertion due, presumably, to a rupture of the fibrous union. It would seem that solid union is necessary before an individual may return to active, competitive sports Excision of the fragment may be necessary if separation has prevented bony union An individual who does not resume active sports may remain completely asymptomatic with a fibrous union and need no further treatment.

In both of these cases only the detached portion of the apophysis was removed. No attempt was made to smooth the irregular border of the epiphysis because only the detached fragment seems to cause pain. This apophysis can be avulsed by a sudden stretching of the hamstring muscles or it can be separated by direct trauma. Why this is not more frequent is not clear. For example, in cerebral palsy with hamstring muscle spasm, this condition conceivably might occur, yet it apparently is not reported.

Abnormalities of the development of epiphyses are considered under the general term of osteochondroses. Dr. Charles W. Goff[3] has studied and further classified these as being derived from (1) pressure epiphyses, (2) traction epiphyses, (3) atavistic epiphyses. From the pressure epiphyses are seen *true* types of osteochondroses such as Freiberg's, Kohler's and Calvé's and, most important, the Legg-Calvé-Perthes syndrome. Much study has been given to etiology. The factors usually stated have to do with trauma, infections, endocrine disturbances and nutritional factors. In Goff's series growth charts of 152 children and youths with Legg-Calvé-Perthes syndrome and other true osteochondroses showed that the children with Legg-Calvé-Perthes syndrome had depressed growth prior to and after the onset of this disorder.

The *false* osteochondroses occur in normally developing children and involve the traction and the atavistic epiphyses, as seen in Osgood-Schlatter's disease and the ischial tuberosity which we are discussing. Trauma seems to be the only etiologic factor operating to cause these distubrances. One might conjecture as to whether or not unknown growth factors may influence both the true and the false osteochondroses.

Dr. J. E. Markee and associates[6] have demonstrated that muscles extending across both the hip and the knee joint have multiple levels of nerve supply. When these nerves are stimulated individually an isolated segment of muscle will contract, and at the

same time the other areas of the muscle will stretch. In such muscles simultaneous contractions and stretching may occur. This may be a factor in diminishing the shock forced on the hamstring muscles during a maximum effort and, likewise, may be a factor in minimizing the incidence of this disorder.

The mechanism, symptoms and roentgenographic findings are characteristic, and the clinical course is predictable, varying only with the degree of separation of the fragment. We hope that these 2 cases, together with a review of the condition, will promote a more widespread recognition of this injury and a better understanding of its etiology and treatment.

REFERENCES

1. Abbate, C. C.: Avulsion fracture of the ischial tuberosity; a case report, J. Bone & Joint Surg. 27:716-717, 1945.
2. Berry, J. M.: Fractures of the tuberosity of the ischium, J.A.M.A. 59:1450, 1912.
3. Goff, C. W.: Legg-Calvé-Perthes syndrome, Springfield, Ill., Thomas, 1954.
4. Labuz, E. F.: Avulsion of the ischial tuberosity, J. Bone & Joint Surg. 28:388, 1946.
5. McMaster, P. E.: Epiphysitis of the ischial tuberosity; a case report, J. Bone & Joint Surg. 27:493, 1945.
6. Markee, J. E.: Two-joint muscles of the thigh, J. Bone & Joint Surg. 37A:125-142, 1955.
7. Milch, H.: Ischial Apophysiolysis—A New Syndrome *in* De Palma, A. (ed.): Clinical Orthopaedics, No. 2, p. 184, Philadelphia, Lippincott, 1953.
8. Scott, W.: Non-union of the ischial tuberosity associated with epiphysitis vertebrae, J. Bone & Joint Surg. 28:862, 1946.
9. Watson-Jones, R.: Fractures and Joint Injuries, ed. 3, p. 372, Baltimore, Williams & Wilkins, 1943.
10. Winkler, H., and Rapp, I. H.: Ununited epiphysis of the ischium, J. Bone & Joint Surg. 29:235, 1947.

Evulsion del Epiphyse Ischial

Summario in Interlingua

Proque separation del tuberositate del ischio se trova reportate in le litteratura in minus que vinte casos, nos crede que il vale le pena describer duo casos que occurreva in duo pueros in le secunde decennio de lor vita e que ambes requireva interventiones chirurgic. In un de iste patientes, le examine roentgenologic suggereva un forte suspicion de chondrosarcoma. Iste condition occurre usualmente in pueros durante lor adolescentia e affice le plus communmente le tuberositate al latere sinistre. Le sol significative observation clinic esseva un persistente spasmo muscular e dolor durante palpation profunde super le tuberositate del ischio. Le duo pueros non respondeva a prolongate periodos de tractamento supportative, incluse allectamento. Ambes se presentava a nos proque illes poteva non plus participar in activitates athletic.

Ambe iste patientes experientiava un prompte alleviamento de lor symptomas post le excision de un grande portion del epiphyse. In un del casos le fragmento consisteva predominantemente de cartilagine, in le altere de osso.

Nos desira presentar un revista del mechanismo possibile que effectua le production de iste lesion. Nos include in nostre reporto certe datos contribuite per previe autores. Nos spera que le presente articulo promove le appreciation de iste condition e contribue al establimento de un plano de tractamento.

22

Ankle Fusion in the Absence of Talar Body

ELIHU FRIEDMANN, M.D.,* AND JACK DUNN, M.D.†

Arthrodesis of the tibia to the os calcis in the absence of the body of the talus always has presented a technical surgical problem. The use of an inverted fibula graft is hereby presented as another approach to obtaining fusion in such cases.

The technic is a variation of the fusion described by Adams‡ in which an osteotomy of the fibula is performed above the ankle joint, and an onlay fibula graft is screwed to the tibia and the talus after the articular cartilage of the ankle has been removed. In the case presented this procedure could not be used because the cortex of the os calcis projected lateral to the tibia, causing the graft to be held away from the lower portion of the tibia when in contact with both bones. Therefore, to obtain satisfactory approximation to the 2 bones involved, the fibular

* Attending in Orthopedic Surgery, Veterans Hospital, Wilkes-Barre, Pa.

† Assistant Chief, Surgical Service, Veterans Hospital, Wilkes-Barre, Pa.

‡ Adams, J. Crawford: Arthrodesis of the ankle joint, experiences with the transfibular approach, J. Bone & Joint Surg 30B:506, 1948.

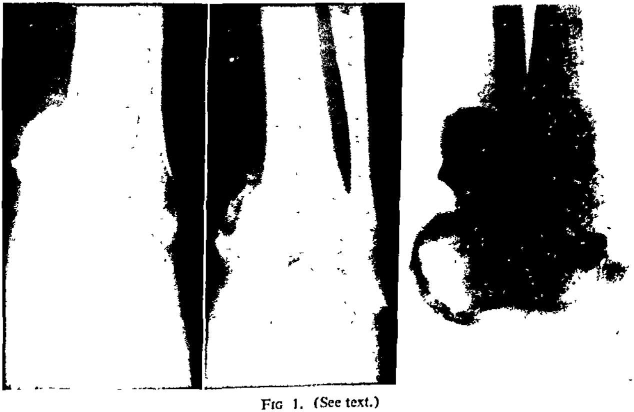


FIG 1. (See text.)

graft was rotated 180°, permitting the cylindrical shaft to fit into a drill hole in the os calcis and the flattened fibular malleolus to rest against the lateral cortex of the tibia.

CASE REPORT

The patient was a 25-year-old white male who, on June 1, 1953, was involved in a motorcycle accident and sustained a compound fracture of the right ankle. Emergency hospitalization for 11 days was provided elsewhere, and conservative treatment was given. This included several débridements of a draining area on the medial aspect of the right ankle.

On October 16, 1953, the patient was transferred to the Veterans Administration Hospital, Wilkes-Barre, Pa. He presented a 1-cm. draining sinus on the medial aspect of the right ankle with surrounding granulation tissue and erythema, marked atrophy of the right thigh, the calf and the right ankle region, and skin changes secondary to prolonged casting of the leg. A small amount of seropurulent material was noted in the sinus opening. Ankle motion was markedly limited and painful. Considerable firm swelling of the ankle was present. The temperature was not elevated. The remainder of the physical examination revealed no significant abnormalities.

Roentgen examination revealed a fracture of the neck of the right talus. The body of the talus was displaced medially out of the joint and rotated. It rested in the region of the Achilles



FIG 2. (See text)

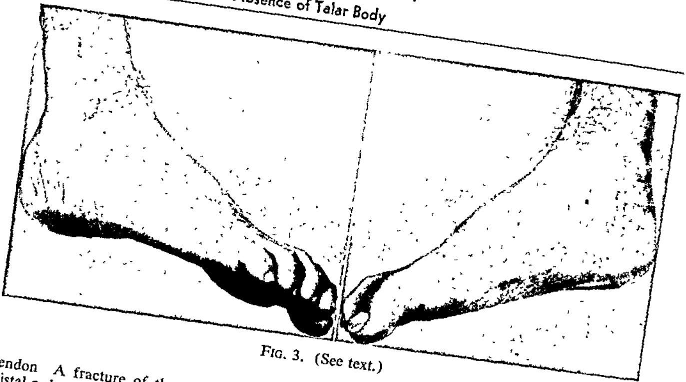


FIG. 3. (See text.)

tendon A fracture of the anterior lip of the distal right tibia, extending into the ankle joint, was also present (Fig. 1).

The routine hemogram, urinalysis and serology all were within normal limits. The patient had a satisfactory protein level, and the urea nitrogen was reported as 15.5 mg per cent.

With conservative treatment, the sinus area eventually closed, and the inflammatory reaction subsided.

TECHNIC

On February 4, 1954, a fusion of the right ankle was done (Fig. 2) under general anesthesia with pneumatic tourniquet technic. Through a lateral incision, dissection was carried down to the fibula, which was osteotomized about 4 inches from its malleolar tip and completely removed from the wound. The body of the talus, which had been dislocated posteriorly, then was dissected free and removed. This bone showed definite evidence of aseptic necrosis. Bone chips were placed between the os calcis and the tibia after articular cartilage had been removed The medial cortex of the fibula was removed in preparation for its use as a bone graft Then the osteotomized portion of the fibula was rotated 180°, and its cylindrical shaft was inserted into a hole prepared for it through the dorsum of the os calcis. Next, the malleolar portion was fixed to the lateral aspect of the tibia with a screw, and the wound was closed in routine fashion. A plaster of Paris cast was applied.

The postoperative course was uneventful except for the appearance of an ulcerated area at the site of the inserted screw. On March 15, 1954, the screw was removed from the right ankle. Immobilization in plaster was continued until roentgenographic evidence of satisfactory ankle fusion was obtained and confirmed by "push-pull" roentgenographic studies on August 11, 1954. With physiotherapy the patient went on to subsequent weight-bearing without symptoms. By March 15, 1955, the patient was bearing weight without discomfort and, clinically, presented a satisfactorily fused ankle (Fig. 3). All wounds were dry and well healed. The patient returned on April 5, 1955, presenting, again, a recurrent ulceration on the scarred area of the right ankle. Again, with conservative treatment, the lesion subsided Ambulation was resumed, and the patient, at present, is without discomfort. The last check roentgenogram made on April 5, 1955, again confirmed the presence of satisfactory fusion.

SUMMARY

A case has been presented to demonstrate a technic for ankle fusion in the absence of the body of the talus, using an inverted fibular graft.

Arthrodese del Tibia al Calcaneo in le Absentia del Corpore del Astragalo

Summario in Interlingua

Es presentate un technica pro le arthrodese del tibia al calcaneo in le absentia del corpore del astragalo. Un invertite graffo fibular esseva inserite in un cavo forate in le portion superior del calcaneo e fixate al aspecto lateral del tibia. Le graffo ossee representava un ponte que promoveva le fusion.

Section III

Motorist Injuries and Motorist Safety

PRIMARY MOTORIST SAFETY: PREVENTION OF ACCIDENTS
(Part 3)

Guest Editor: JACOB KULOWSKI, M.D.
Saint Joseph, Missouri

Acknowledgments

I wish to thank Dr. Anthony F. DePalma for making possible the presentation of this project to those in the field of medicine. Without his appreciation of the value of this symposium and his co-operation in his editorial capacity it could never have been. To all the authors who have participated I am deeply obligated for work done in the best traditions of science and humanity. I am also indebted to Mr. Carl Brill, whose stature as a medical illustrator has long been established; to Miss Ruth McNulty, medical record librarian of the Missouri Methodist Hospital; and to Mrs. Mary Margaret Sittel for her special interest and her forbearance during the earlier and most trying periods of preparation for the publishers. J. B. Lippincott Company, as was to be expected, has been meticulous in the handling of this material. Last, but not least, I am grateful to Margaret, my wife, for her unflagging interest in traffic problems and her help in the preparation of all the material.

Jacob Kulowski, M.D.
Guest Editor

1

Introduction: Prevention of Accidents

Jacob Kulowski, M.D.

Let the mind rise from victory to victory over surrounding nature . . . yet the same human creature . . . produces for itself . . . losses and pain . . . science . . . will purge him from his contemporary shame in the sphere of interhuman relations.

—Pavlov

Born of violence, the problems of motorist accidents have developed a dynamic concept and unifying effect upon individuals and groups who are trying to bring these casualties under control. This is the more remarkable because motoring accidents comprise only one particular facet of the "traffic problem." In point of fact this problem itself is actually the sum total of several problems: congestion and delay; lack of terminal or parking facilities; and traffic accidents. The incredible growth of motor-vehicle transportation helps to explain the magnitude of this problem. In the past 55 years our population has doubled (64% urban), but the number of motor vehicles has increased more than 7,000 fold. It also helps to explain why this symposium has concentrated upon motorist accidents as distinguished from pedestrian accidents.

Above all, this staggering accident and injury potential continues to underscore the fundamental nature of primary accident prevention Accident prevention has been the special field of endeavor of the National Safety Council for many years. The efforts of this admirable organization have culminated in its famed tridimensional approach to the problem: the three E's, or Education, Enforcement and Engineering. On this basis or classification and isolation of the various parts of this area of motorist safety, prevention has been raised to a very high point as an art. Can this art be transformed into a more effective and vigorous science?

The answer to this question is bound inevitably to answers to the question, Why do accidents occur? Thus far the latter are absent, scarce or controversial. There is a real need for research to determine which human and/or inhuman faults or failures cause greater-than-chance accidents. In the same way that the how of injury production is being clarified by crash-impact engineering studies, so must the why of accident occurrence be amplified through valid investigative findings along these lines. Admittedly this phase of the problem may be more difficult to pursue and prove. However, some work is in progress through epidemiologic technics. In the meantime there is much to be said from the standpoint of intuitive and deductive thinking and on the basis of common experience. Until more valid data are forthcoming to bridge existing gaps in our knowledge, the beginnings and the early development of progress along lines of accident prevention will have to be made on this basis.

This kind of intelligence never should be underestimated anyway. Good examples of the validity of such thinking are furnished by uncontrolled fast driving and drunken driving, in regard to which accumulating data overwhelmingly support previously held

opinions that speed is the number one killer; also, that drunken driving is the number one cause of accidents.

This statement and common experience support the opinion held generally that the "behavior of the driver en masse" determines largely the results of motor-vehicle transport from the standpoint of accidents and injuries. If that is true, then the chief efforts toward alleviating the accident problem must be concentrated upon this not-so-mythical driver. The magnitude of the problem looms ever greater in view of the increasing gap between automotive advances and human capabilities to cope with them.

The point to remember with regard to this phase of motorist safety is this: primary safety is dependent upon the relationships that exist (and that can be altered within certain limitations) among the driver (and other drivers), his vehicle (and other vehicles about him) and the immediate highway facility (as well as that at intersections). Even thus categorically stated, the importance of driver proficiency (education, training and psychosomatic fitness), enforcement and engineering cannot be dimmed. All have to be integrated. Until engineers can offset the element of human error, however, enforcement will gain inevitably in scope and effectiveness in any program of accident control.

Enforcement—as defined by the International Association of Chiefs of Police (ICAP) and approved at its 1950 conference—means compelling obedience to statutes and ordinances by citation or arrest and penalization for disobedience of such regulation This applies to statutes, ordinances and legally authorized regulations relating to the use of streets and highways, to ownership and operation of motor vehicles. In a general way this involves two official functions: (1) police traffic law enforcement—the detection and apprehension of violators; and (2) court traffic law enforcement—prosecution, adjudication and penalization of violators.

In the past police traffic law enforcement has been greatly misunderstood—and unjustly feared by many motorists because of some unfair practices with regard to so-called speed traps in some localities. This has been overcome largely by modern police policies toward informing the public in advance when crack-downs are to be made against unsafe driving practices. Also, by this attitude the police gain the deterrent effects that they wanted in the first place.

A part of driver education should be the indoctrination of individuals that the safety and the welfare of a community are the basic responsibility of the police. Since accident experience is a constant threat to the entire community, police traffic law enforcement is a basic police function.

The purpose of traffic law enforcement is to induce safe, legal driving habits through proper conduct and self-discipline by deterrents adequate enough to enforce compliance with regulations even when there is no one on the spot to uphold the law. Effects sought, therefore, are direct (on the violators) and indirect (for some potential violators). This idea may be based upon the well-known principle of conditioned reflexes But admittedly it is true that under present conditions self-imposed deterrents, such as fear of accidents, sense of social responsibility, pride in one's driving record of safety, etc., are not enough and must be bolstered by traffic law enforcement in order to help keep accidents to a tolerable level.

Be that as it may, the gradual encroachment of enforcement is a sobering thought to both officials and the driving population—or it should be. This trend, however essential it may appear to be, can be minimized through adequate standards of driver licensure, as well as improved automotive and traffic engineering.

The medical aspects of driver licensure are considered elsewhere.

Automotive safety engineering and design have already been discussed at some length. Human engineering has been defined. What about the traffic engineer?

The limitations of drivers—and vehicles—are being taken into consideration by highway engineers and designers. The concept here is dynamic as well as geometric. The magnitude of this facet of the problem also has led to the development of so-called traffic engineers. By official definition traffic engineering is

> that phase of engineering which deals with the planning and geometric design of streets, highways and abutting lands, as their use is related to safe, convenient and economic transportation of persons and goods.

Thus the mixture of human behavior and the physical laws of time, space and motion permeates the thinking and the planning of traffic engineers (as it must also all individuals and groups interested in traffic safety). In a general way their efforts involve "constructive" and "regulatory" methods. Regulatory methods (in addition to those of the police and courts of law) seek to control road-user behavior to meet the conditions of traffic and the physical limitations of the road.

It is evident, even from this brief introduction, that accident prevention—like reduction of injuries and aids to recovery—requires a multifaceted approach. As progress is made, the real and the imagined frontiers of these different methods will tend to disappear into the whole endeavor. Principles and philosophy have been established. Theories have been pronounced; correlations are needed to make these work. This will advance us another step toward the quantitative stages of traffic safety control and development. This ultimate goal will probably derive from the domain of engineering. Its essence will be the reduction of driver-critical decisions. Put another way, this means making dangerous acts *impossible* and right ones easier and more natural.

All this is predicated upon the fact that drivers have certain natural limitations with regard to reaction time, power of judgment and power of observation. For this reason alone it is necessary to establish minimal standards of driver licensure. The need in regard to those actually handicapped psychosomatically becomes even more urgent from this viewpoint. This should be introduced first on a voluntary basis, in the democratic tradition. It may be that introduction of this kind of curtailment with the "fifth freedom" might lead to an honest nation-wide participation in motoring self-preservation.

But all this takes time and treasure, and time is taking an increasing toll of life and limb from the American driving population. Until the ideal envisioned above can be attained, another stopgap must be put to work—Enforcement. The state of Connecticut is proving that a sound traffic enforcement program saves lives.*

On this subject the words of Mr. Boate serve well to end this chapter:

> . . . a strict traffic law enforcement program . . . using suspension of the driving privilege . . . brings about an immediate reduction of traffic accidents, injuries and deaths. There is also evidence that the vast majority of the public does not oppose strict enforcement programs, but actually seeks the protection they afford. . . . The Connecticut program . . . is credited with being largely responsible for a 14% decrease in that state's traffic fatalities during the first quarter of 1956. . . . The Connecticut reduction . . . was made . . . when accident experience increased by 11% in all other parts of the nation. Under the Connecticut enforcement program, the operating licenses of all convicted speeders are suspended 30 days for the first offense and 60 days for the second offense. . . . Since the introduction of the strict enforcement program in Connecticut, the number of arrests . . . has decreased.

The Connecticut program, and earlier programs, prove two things: first, that a successful method for immediately reducing traffic accidents, injuries and fatalities does exist; and, second, that the public accepts firm and impartial enforcement. *All that remains is for state officials to adopt policies of strict enforcement and driver control through license suspension.*

* Connecticut Proves Traffic Law Enforcement Saves Lives (Brass Button 5:1, 1956—Thomas N. Boate, Mgr., Accident Prevention Dept., Assn. of Casualty and Surety Companies).

BIBLIOGRAPHY AND OTHER SOURCES OF SAFETY INFORMATION

Accident Facts: National Safety Council, 425 N. Michigan Ave., Chicago 11, Ill., 1956.

Aeromedical Field Lab., Holloman Air Development Center, Holloman Air Force Base, New Mexico.

Air Research and Development Command, Commander, Att.: RDTRH, P.O. Box 1395, Baltimore 3, Md.

Air University Library, Director, Maxwell Air Force Base, Alabama

American Association of Motor Vehicle Administrators, Woodward Bldg., Washington, D.C.

American Automobile Association, Educational Consultant, Washington, D.C.

American College of Surgeons, Department of Literary Research, 40 E. Erie St., Chicago, Ill.

A.M.A. Committee on Automobile Crash Injuries and Deaths, Chairman, Charlottesville, Va.

American Road Builders Association, National Press Bldg., Washington, D.C.

American Society of Civil Engineers, 33 W. 39th St , New York, N.Y.

Armed Forces Epidemiological Board, Executive Secretary, Office of the Surgeon General, Department of the Army, Washington 25, D C.

Armed Forces Medical Library, Washington, D.C.

Armed Forces Technical Information Agency, Documents Service Center, U.B Bldg., Dayton 2, Ohio.

Association of Casualty and Surety Companies, Accident Prevention Department, 60 John St , New York, N.Y

Aston, J. M , and Perkins, J. A : The clinical pattern of injury in road accidents, Brit M. J. 2:200, 1954.

Automobile Manufacturer's Association, New Center Bldg., Detroit 2, Mich.

Automobile Safety Foundation, 200 Ring Bldg., Washington 6, D.C.

Automotive Crash Injury Research, Cornell University Medical College, 316 E. 61st St , New York, N.Y.

Bastow, D Vehicle design; for road safety, Engineering 178:370, 1954.

Center for Safety Education, New York University, Washington Square, New York, N.Y.

Chrysler Corporation, Engineering Division, P O Box 1118, Detroit 31, Mich.

Crash Injury Research, Cornell University, Division of Aviation, LaGuardia Field, Marine Area Terminal, Flushing 71, N.Y.

Current Topics in Traffic Safety, National Safety Council, vol. 27, 1955.

Dempster, W. T.: Space requirements of the seated operator, Project No. 7214 WADC, Tech. Report 55-159, Wright Air Development Center, July, 1955.

Department of the Air Force, Executive Office, Directorate of Research and Development, Washington 25, D C.

Department of Motor Vehicles (Chief of Division), Division of Driver's Licenses, State of California, Sacramento 2, Cal.

Dye, E. R., and Smith, A. C.: Automobile Seat Belts; A Way of Living, Buffalo, N.Y., Cornell Aeronautical Lab , Inc., 1955.

Eastwood, W. J., and Jefferson, G : Discussion on fractures and dislocations of the cervical vertebrae, Proc. Roy. Soc. Med. 33:651, 1940.

Edwards, J. A.: Automobile impact studies, Automobile Eng. 46:215, 1956

Elliott, H.: Medical research in traffic accidents, a plan for studying the problem through research units in casualty wards of teaching hospitals, Canad M. A. J. 74:557, 1956.

Engineering and Research Division, Chief, Office of Assistant for Ground Safety, DCS/P, Department of the Air Force, Washington 25, D C.

Flecton, the pedestrian protection, Traffic Eng 26:36, 1955

Freedom of the American Road, Detroit, Ford Motor Company, 1956.

Gay, J. R.: Minor injuries of the spinal column caused by traffic accidents, Canad Services M J. 12:131, 1956.

Gerlough, D. L · Instrumentation for automobile crash injury research, J. Instrum. Soc. America 1:29, 1954

Grossjohann, A.. The medical examination of drivers of motor vehicles, Deutsch. med Wasch. 79:1294, 1954 (English abstr. in Road Abstracts).

Guyahoga County, Coroner's Office, 2121 Adelbert Rd , Cleveland, Ohio.

Haack, M.. Human tolerances to vibrations in farm machinery, Agric Eng 37:253, 1956

Halsey, M.: Traffic Accidents and Congestion, London, Chapman & Hall, 1941.

Harvard School of Public Health, 695 Huntington Ave., Boston, Mass.

H M. Stationery Office, Metropolitan Police Driving School, Manual of Driving Instruction for Students of the Motor Car Wings, London, England.

Indiana State Police Auto Crash Injury Research, Stout Field, Indianapolis, Ind.

Institute of Traffic Engineering, 2029 K St., N.W., Washington 6, D.C.

Institute of Traffic Engineers, 60 John St., New York, N.Y.

Institute of Transportation and Traffic Engineering (ITTE), 465 Hilgard Ave., Los Angeles 24 (University of California), Cal.

Jenkins, Sir George: Safety in transport, J. Inst. Trans. 26:3, 1954.

Kraft, M.: Driver Control, Eno Foundation for Highway Traffic Control, Sangatuk, Conn., 1954.

McFarland, R. A., *et al.*: Human Variables in Motor Vehicle Accidents; A Review of the Literature, Cambridge, Mass., Harvard School of Public Health.

Matson, T. M., Smith, W. S., and Hurd, F. W.: Traffic Engineering, New York, McGraw-Hill, 1955.

Moede, W.: Aptitude test for drivers, Ztschr. Verkehrssicherheit 2:3, 1954.

Moore, M., Jr.: Immediate care of automobile accident victim, Journal-Lancet 75:445, 1955.

Motor Vehicle Research, Inc., New Market, So Lee, New Hampshire

National Research Council, Division of Engineering and Industrial Research, Washington, D.C.

National Safety Congress, 43rd General Session, vol. 1, 1955.

Package Library of the A.M A., 535 N. Dearborn St, Chicago 10, Ill.

Proceedings of the Highway Research Board, 2121 Constitution Ave., Washington, D C.

Protection, Inc., 6521 West Blvd., Inglewood 3, Cal.

Quarck, H.: Attitude of the road user with regard to safety at level crossings (RR), Bundesbohn 29:1087, 1956.

Randolph Field School of Aviation, San Antonio, Tex.

Road Research Laboratory, Director of Road Research, Harmondsworth, West Drayton, Middlesex, England

Safety Glass Association, Inc., Executive Director, 118 E. Main St., Hillsboro, Ohio.

Schwarz, F.: The medical examination of motor drivers, Ztschr. Verkehrssicherheit 2:195, 1954.

[illegible] Technical [illegible] ct Studies, [illegible] ich., January 9-13, 1956.

Society of Automotive Engineers (SAE), 29 W. 39th St., New York, N.Y.

Special Subcommittee on Traffic Safety, Congress of the United States, House of Representatives, House Office Bldg., Washington, D.C.

Stadie, A.: Death and casualty rates increased after abolition of speed limit in Germany, Deutsche Strassenverkehr 4:97, 1954.

Starks, H. J. H.: Toughened glass; investigations into some safety aspects, Automobile Eng. 44: 433, 1954.

Stonex, K. A.: Relation between automobile and highway, Res. Bd. Washington 33:91, 1954.

Syrek, D.: Accident rates at intersections, Traffic Eng. 25:312, 1955.

Tonti, D. L.: Lowered accident rate due to improved design of New Jersey Garden State Parkway, Better Roads 25:28, 1955.

Traffic Institute, Northwestern University, 1704 Judson Ave., Evanston, Ill.

Traffic Safety Association of Chicago, Chicago, Ill.

Traffic Safety Association of Detroit, Detroit, Mich.

Traffic Safety and Highway Improvement Department, Ford Motor Company, 3000 Schaefer Rd., Dearborn, Mich.

Vehicle Safety Section, Engineering Staff, General Motors Corporation, G.M. Tech. Center, Detroit 2, Mich.

Wayne University, Board of Education, Detroit, Mich.

Wright Air Development Center, Commander, Att.:WCRB, Wright Patterson Air Force Base, Ohio.

reverse, if we are to hold the line in 1966 at the 1955 and 1956 death totals of 38,300 and 40,000, the exposure death rate 10 years hence will have to decrease approximately one third to 4.6.

This is the highway safety situation confronting the nation's traffic authorities and citizens during the next 10 years.

COMPLEX PROBLEM

By its very nature highway transportation is one of the most complex government-citizen problems today. It concerns not only the economy of the country and its defense mobility in the event of enemy attack but, most importantly, the safety and the welfare of the people. It involves the laws of nature, including time, space and motion plus the frailties and the complexities of human nature and the interrelations and the competition of human beings living together. When one reflects upon all the shortcomings of human beings, his own driving experience and the freedom inherent in motor-vehicle travel, the wonder is that the accident experience is not many times that currently recorded.

ENVIRONMENT AND MOTIVATION

In recent years much has been written and spoken about the three "E's" of traffic safety—Engineering, Enforcement and Education. All three, of course, are necessary and important, and without proper application in the degree necessary of each of the three the traffic accident problem cannot be curtailed permanently.

It is neither the intent nor the desire to oversimplify the problem; nor is it possible to sum up in a few words a solution to our traffic difficulties. However, from the operational viewpoint, it is possible to consolidate in two words the broad basic approaches of attack for traffic safety improvement: *Environment* (improved), lessening the importance of the human element factor; and *Motivation* (proper), encouraging through education and supervision good highway habits and proper attitudes on the part of all highway users.

Each of these two broad approaches involves many kinds and facets of activity and endeavor, some in one field, some in the other, while still others concern environment as well as motivation. Collectively, all these activities make up the action program sponsored by the President's Committee for Traffic Safety, endorsed and supported by traffic authorities, as well as by national traffic organizations.

Space does not permit of a detailed discussion of all the elements that make up these two approaches. Suffice it to say, however, that Environment, in the broad sense, concerns all those things of a scientific and engineering nature that make it less possible for highway users to become involved in accidents despite the frailties of human beings. These include highway and motor-vehicle design and maintenance, traffic engineering and the realistic application of regulations and restrictions. Motivation factors, on the other hand, are in many respects less exacting from the scientific point of view. They are, however, equally important and not only concern informational and educational endeavors designed to improve user habits and attitudes from the standpoint of instruction and moral suasion but also include authoritative control, supervision and punishment serving as deterents to improper roadway use causing accidents.

ENGINEERING DESIGN

The effectiveness of environmental improvements has been well illustrated in the past, and especially in recent years. Specifically, the design changes in the automobile and the highway have proved their worth, not alone in the area of more comfortable and more expeditious traffic movement but, most importantly, in the potential and actual reduction of accidents through automatic features of design, construction and control. For example, the mere physical segregation of opposing flows of traffic along multilane

2

Driver Proficiency

Arnold H. Vey*

"Man is still the greatest miracle and the greatest problem on this earth," said David Sarnoff, Chairman of the Board of the Radio Corporation of America, as he sent the first message ever transmitted with electricity obtained by direct conversion of atomic energy.

This seemingly self-contradictory statement is especially true in the field of highway transportation. Through man's foresight and inventive talents, the motor vehicle has become not only a most popular means of travel but a form of transportation essential to present-day living. However, man has not been equally skillful in controlling the safe and proficient use of the motor vehicle.

As proof of this paradox one need only cite the traffic accident record rolled up annually on the streets and the highways of the nation—38,300 dead during 1955, another 1,350,000 injured and an estimated economic loss of 4½ billion dollars. This is the casualty and dollar-loss record for one year only, and unless the tide is turned the prospect is higher totals in the years ahead.

Through the years, particularly since World War II, we have pointed with some degree of pride to the decreasing motor-vehicle death rate based upon exposure. For example, in the past 20 years, for each 100 million miles of motor-vehicle travel, traffic deaths have declined from 15.9 to 6.4. Truly an admirable record! But what of the upward of 40,000 citizens killed needlessly in each recent year? Are they an inevitable price for advancement in mobility? Of more importance, what does the future hold in store?

It is estimated that by 1966, barring an extended economic depression or outbreak of war, the present 62 million registered vehicles will increase to 82 million, and motor-vehicle travel will increase from 595 billion miles to 825 billion miles—a jump of nearly 40 per cent.

Incidentally, the past two years saw a reversal of the previously yearly declining death rate—6.4 in 1955 and 1956 compared with 6.3 during 1954.

If, in 1966, the 1955 and 1956 death rate of 6.4 should prevail, the total number of deaths would equal 53,000—based upon estimated travel for that year. Or, stated in

---

* Formerly Manager, Traffic and Transportation Department, National Safety Council. Now engaged temporarily in a consultative capacity with Simpson & Curtin, Transportation Engineers, Philadelphia, Pa.

(This symposium on Motorist Injuries and Motorist Safety certainly reflects editorial prejudices. However, the results of the participating authors have justified and given spirit to these hopes and beliefs. Nowhere is this more apparent than in what Mr Vey has to say, both as an individual and as a representative of the great family of men and women who make up the National Safety Council's central organization. The successes of this body's fight for life are evident in many ways. Some are obvious, others are not. Among the latter is the ever-widening scope of and interest in safety in every segment of our daily existence. This has called for dedication to one's job and ideals of the highest caliber. Arnold Vey qualifies on both counts.

Nothing can be accomplished until knowledge is assimilated, classified and defined in terms which can be translated into action. Mr Vey has done this most incisively. His words give promise because of the thought-provoking analysis he has written. But students of safety have learned to expect this sort of thinking and communicating from members of the National Safety Council. (Ed.))

reverse, if we are to hold the line in 1966 at the 1955 and 1956 death totals of 38,300 and 40,000, the exposure death rate 10 years hence will have to decrease approximately one third to 4.6.

This is the highway safety situation confronting the nation's traffic authorities and citizens during the next 10 years.

COMPLEX PROBLEM

By its very nature highway transportation is one of the most complex government-citizen problems today. It concerns not only the economy of the country and its defense mobility in the event of enemy attack but, most importantly, the safety and the welfare of the people. It involves the laws of nature, including time, space and motion plus the frailties and the complexities of human nature and the interrelations and the competition of human beings living together. When one reflects upon all the shortcomings of human beings, his own driving experience and the freedom inherent in motor-vehicle travel, the wonder is that the accident experience is not many times that currently recorded.

ENVIRONMENT AND MOTIVATION

In recent years much has been written and spoken about the three "E's" of traffic safety—Engineering, Enforcement and Education. All three, of course, are necessary and important, and without proper application in the degree necessary of each of the three the traffic accident problem cannot be curtailed permanently.

It is neither the intent nor the desire to oversimplify the problem; nor is it possible to sum up in a few words a solution to our traffic difficulties. However, from the operational viewpoint, it is possible to consolidate in two words the broad basic approaches of attack for traffic safety improvement: *Environment* (improved), lessening the importance of the human element factor; and *Motivation* (proper), encouraging through education and supervision good highway habits and proper attitudes on the part of all highway users.

Each of these two broad approaches involves many kinds and facets of activity and endeavor, some in one field, some in the other, while still others concern environment as well as motivation. Collectively, all these activities make up the action program sponsored by the President's Committee for Traffic Safety, endorsed and supported by traffic authorities, as well as by national traffic organizations.

Space does not permit of a detailed discussion of all the elements that make up these two approaches. Suffice it to say, however, that Environment, in the broad sense, concerns all those things of a scientific and engineering nature that make it less possible for highway users to become involved in accidents despite the frailties of human beings. These include highway and motor-vehicle design and maintenance, traffic engineering and the realistic application of regulations and restrictions. Motivation factors, on the other hand, are in many respects less exacting from the scientific point of view. They are, however, equally important and not only concern informational and educational endeavors designed to improve user habits and attitudes from the standpoint of instruction and moral suasion but also include authoritative control, supervision and punishment serving as deterents to improper roadway use causing accidents.

ENGINEERING DESIGN

The effectiveness of environmental improvements has been well illustrated in the past, and especially in recent years. Specifically, the design changes in the automobile and the highway have proved their worth, not alone in the area of more comfortable and more expeditious traffic movement but, most importantly, in the potential and actual reduction of accidents through automatic features of design, construction and control. For example, the mere physical segregation of opposing flows of traffic along multilane

roadways by the application of a medial strip of appropriate design lessens substantially the frequency and the consequence of head-on collisions. The present-day expressways of controlled access type have to an even greater extent brought about a larger reduction of accidents by making it less possible for drivers to have accidents despite little, if any, change in driver habits and attitudes through elimination of the many possible vehicular conflicts existing on the older type of roads. Some of the recently constructed turnpikes now are experiencing accident rates of a quarter to a fifth of the rates of the older type of surface roadways subject to frequent marginal and internal conflicts. This despite heavy volumes of traffic moving at times at speeds 30 per cent to 50 per cent higher than on the older type of facilities.

Regardless of these and future environmental improvements, including the possible development and application of electronic vehicular controls, for the immediate future and many years to come the user factor (drivers and pedestrians) will continue to be the greatest challenge in the increasing problem of traffic safety.

THE HUMAN ELEMENT

Because of the place of the automobile in our everyday living and by the very nature of the problem, all of us, except the bedridden and infants, have a concern and a responsibility in the incidence of traffic accidents.

True, for any one year only a small percentage of the nation's licensed drivers are involved in accidents. And, contrary to the belief of some, the bulk of the nation's accident drivers in a single year have never before been involved in a reportable accident, or at least sufficient years have lapsed between accidents so that they are not recorded as accident prone.

Since it has not been possible up to this time to screen out potentially dangerous drivers at the time of initial licensing by means of precise and valid scientific tests, it has been customary to license all comers until such time as they have acquired a bad driving experience of repeated accidents and violations. The few exceptions include those with obvious physical or mental handicaps. The traffic-accident problem, therefore, involves all the elements of human behavior, including physical, mental, emotional and educational, as well as health and medical, factors. To what degree and in what manner these elements and factors are involved, and their interrelation to safe driving, have not yet been determined accurately, and therefore, are subjects for further scientific research and study.

NEED FOR RESEARCH

Why do drivers drive at speeds "too fast for conditions"? Why do drivers "drive to the left of the center line" when approaching hills and curves, despite inadequate sight distance? Why do drivers fail to "obey" regulatory devices erected for their protection? Why do drivers "compete" for the same roadway space in defiance of the common law of physics that two objects cannot occupy the same space at the same time? These and many other questions can be answered only through greater knowledge of human behavior as it relates to the use of the motor vehicle.

Further research in the area of human behavior involves:

Intelligence. An evaluation of the relationship, if any, between intelligence and traffic behavior. *Incidentally, traffic law* knowledge tests have indicated that, by and large, habitual offenders score high in their knowledge of the traffic laws and rules of the road.

Education. The degree to which learning and practicing the skills and the habits of safe driving are interrelated to accidents. This, too, concerns behavior responses related to past experiences and the ability always to react properly in comparable circumstances. For example, "seeing" is not

alone a prerequisite of safe driving; equally important to proper vision is good "seeing habits"—in other words, knowing what is going on around the driver (all four points of the compass)—within vision of driving range, of course—and reacting to avoid conflict with others.

Emotion. The correlation of attitudes, moods, tolerance of others and the complexities of competitive living in a modern world and traffic accidents. Is it a fact that as we live so we drive?

PHYSICAL, HEALTH AND MEDICAL FACTORS

What is the relationship between the physical well-being of drivers and traffic accidents? Should physical examinations be a prerequisite of a driver's license? If so, what are the standards?

To what extent are ailments such as certain heart diseases, diabetes, epilepsy and others related to accident incidences? Are patients under medical care and receiving treatment for these and other ailments a better or worse driver risk than those not receiving treatment?

The use of alcohol and stimulating drugs, such as barbituates, and their relationship to the incidence of accidents warrant further study.

CONCLUSION

Since the advent of the motor vehicle and its rapid growth in popularity, traffic authorities and others have learned much about the broad aspects of the problem, including knowledge of circumstances and situations surrounding accident occurrence. This knowledge has brought about the development and the application of substantial correctives which in a broad sense have proved their effectiveness. The "Action Program," sponsored by the President's Committee for Traffic Safety and backed by traffic authorities, for example, well illustrates this fact. However, for further improvement there is need not only of more intensive and realistic application of all the elements of the "Action Program" in practically every jurisdiction of the nation but particularly of greater knowledge of man—his capabilities and his shortcomings as they relate to the safe and expeditious use of streets and highways.

Specifically, we are in need of more extensive and accurate evaluation of accident causes related to human factors—the susceptibility of man to accidents, the human and the physical elements involved, and their degree of importance.

Next, we need to know more about accident-prevention measures, their application related to the fundamental principles of the laws of nature, the human characteristics of highway users and predriving as well as inservice screening and training of drivers.

This is a field for constructive research not alone by government but by individuals and organizations able and willing to participate in this most important humanitarian social and economic problem facing the nation.

3

Human Engineering and Automobile Safety

Ross A. McFarland, Ph.D., Sc.D.*

INTRODUCTION

A new discipline has been developing in recent years in which the engineering and the biologic sciences are being integrated. This field of study is commonly referred to as human engineering or biotechnology. One of its primary objectives is to improve safety by designing equipment in terms of human capabilities and limitations.[13] From the standpoint of human engineering, it is essential that the mechanical design of automotive equipment be related intimately to the biologic and the psychological characteristics of the drivers. The effectiveness of the man-machine combination can be greatly enhanced by treating the operator and an automobile as a unified system Thus, instruments should be considered as extensions of the driver's nervous and perceptive systems, and controls as extensions of the hands and the feet regarded as simple tools. Otherwise, it is hardly fair to attribute so many accidents to human failure alone, as is usually done. If motor vehicles are designed from the driver outward, there should be fewer errors in operation and a reduction in accidents.

To state the problem more specifically, it seems reasonable to expect that the design of equipment should be based on an understanding of the sense organs and the characteristics of human perception if satisfactory information is to be supplied from sounds and lights in the operation of equipment. For example, auditory signals might be introduced with frequencies difficult to hear, or in a range to penalize the older driver. Illustrations in other sensory fields—for example, vision and tactual sensitivity—will be given in subsequent sections of this chapter. Secondly, the engineer should not make excessive demands upon a driver in regard to the physical responses, that is, in reaching or operating a control or lever. Finally, switches, handles and knobs should be clearly distinguished. Otherwise, an inadvertent operation may occur.

Furthermore, it should also be realized that frequently drivers of automotive equipment are suffering from temporary impairment of functions causing inefficiency, such as fatigue. Also, there may be changes as a result of aging. Thus, the cumulative effects of undue burdens imposed by poor design features are sure to result in an over-all deterioration of driving efficiency and per-

---

* Associate Professor, Harvard School of Public Health, Boston, Massachusetts

(No one else writing in the field of motor-vehicle safety has quite Dr. McFarland's ability to isolate, classify and relate the data relevant to this highly complex subject. He presents admirably a highly convincing argument in favor of the value of human engineering in its relationships to the various phases of accident prevention on our highways. At the same time he manages to word-paint an integrated canvas that embraces all important facets of accident prevention from the human-engineering point of view. Thus, he points out the role of the clinician and medical groups even in this more recent and specialized field of endeavor. All readers interested in traffic safety, and especially the surgeon in industry, will find much to ponder and act upon in this excellent discussion by the world-renowned investigator in the domain of human engineering. [Ed.])

haps lead to an accident. In general, any control which is difficult to reach or operate, any instrument of poor legibility, any seat inducing poor posture or discomfort, or any unnecessary obstruction to vision may contribute directly to an accident because of the difficulty of operation by the driver.[11]

In applying the concepts of human engineering to the design of automotive equipment, there must be an effective working relationship between the engineer and the biologic scientist. Most of the data thus far have been contributed from the fields of psychology, anthropology, biophysics and physiology. Obviously, however, the physician should participate as a member of the team because of his training in the areas mentioned above.

The control of accidents falls within the province of preventive medicine because of the important role played by human variables. Although the host is of primary medical concern, the agent and the environment, if analyzed from the point of view of human engineering, must also be considered in effective preventive measures.[18]

THE ADVANCE ANALYSIS OF AUTOMOTIVE EQUIPMENT FOR DESIGN FAULTS

The concept of design defect is relatively new and unexplored in the automotive field, partly because accident reports have failed to identify this source as a cause of accidents. Design failures may be so subtle that those responsible for reporting accidents may not even be aware of them, particularly if they are not trained in the field of human engineering. An advance analysis should be made, therefore, of all aspects of design involving human behavior. If defects are present, it is only a matter of "time" before some driver "fails" and has an accident. An outline of the principles and the chief considerations in the advance analysis of equipment for design faults is shown in Table 1.[19]

Many examples can be given of the way in which automotive engineers have made

TABLE 1. ADVANCE ANALYSIS OF AUTOMOTIVE EQUIPMENT

I. Operational job analysis:
   1. Requirements of driving
   2. Driver's area in the vehicle
   3. Characteristics of instruments, displays and controls

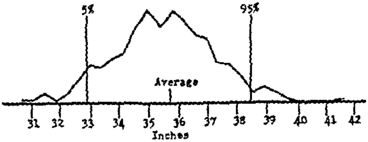
II. Blueprint phase:
   1. Prediction of performance
   2. Human limitations
   3. Anticipation of errors

III. Mockup stage:
   1. Performance of duties
   2. Physical size of drivers
   3. Skill requirements
   4. Age considerations
   5. Interfering structures
   6. Physiologic stress
   7. Errors or near accidents

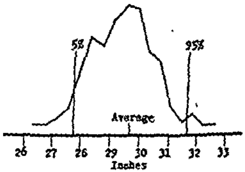
advances to meet human limitations and improve safety. Hydraulic four-wheel brakes, power steering and automatic shifting are excellent examples. However, carefully controlled mockup studies, in which the nature and the range of human abilities can be tested, might aid in making the most of these advances. How fast should the brakes operate in relation to the age, sex, size and strength of the driver? How much "feedback" should be present in the power-steering system, and how should the automatic shifting device be designed for greatest ease of operation and standardization? If the biologic scientist were present during the mockup stages, he might aid the engineer in regard to the ranges of abilities and limitations of the driving population.

The physician, with his background in the biologic sciences, is in an excellent position to recognize errors which have been incorporated in equipment and report them to the automotive engineers for improvement in subsequent models. An extensive research program has been carried out at the Harvard School of Public Health during the past ten years in an attempt to develop essential human-engineering principles in the design of motorized equipment. Representative

Percentiles	Anterior Arm Reach	Knee Height	Sitting Eye Level Height
	Inches	Inches	Inches
5	32.95	20.08	27.72
10	33.46	20.43	28.11
15	33.94	20.63	28.39
20	34.33	20.83	28.58
25	34.65	20.98	28.74
30	34.88	21.18	28.98
35	35.12	21.30	29.13
40	35.32	21.42	29.29
45	35.51	21.58	29.45
50	35.75	21.69	29.61
55	35.94	21.81	29.72
60	36.14	21.93	29.88
65	36.38	22.05	30.00
70	36.58	22.16	30.16
75	36.85	22.24	30.43
80	37.13	22.36	30.55
85	37.44	22.56	30.75
90	37.87	22.84	30.98
95	38.42	23.50	31.61
	Number: 312 Range: 30.66-41.67 Median: 35.75	Number: 301 Range: 19.29-25.98 Median: 21 69	Number: 309 Range: 26.38-32.68 Median: 29.61



Anterior Arm Reach



Normal Sitting Eye Height

FIG. 1. Percentile distributions of ant[illegible] for professional bus and truck drivers. [illegible] Capabilities in the Design and Opera[illegible] School of Public Health)

findings from these and other studies of direct interest to the medical profession are given below.

THE APPLICATION OF HUMAN BODY SIZE DATA TO THE DESIGN OF MOTOR VEHICLES

In order to evaluate vehicles in regard to human-body size, it is necessary to measure not only the dimensions of the vehicles but also the body sizes of the operators. The measurements of the human body necessary for establishing the dimensions of the working space and locating controls are as follows: (a) the maximum arm reaches attainable without altering the position of the body;

(b) the extension of these reaches which can be attained by the movement of the trunk or body; (c) the eye level of the man in the operating position; (d) body dimensions in the operating position, i.e., sitting heights, fore and aft and lateral measurements at various levels; (e) the leg reaches attainable without altering or disrupting posture.[10]

The Use of Static Anthropometric Data

A great deal of human-sizing data has been obtained for pilots in connection with cockpit design, but little specific information is available on motor-vehicle drivers. To acquire these data, an anthropometric team from the Harvard School of Public Health conducted surveys in the field. Measurements of 32 different body dimensions were taken on a representative sample of approximately 400 bus and truck drivers in all parts of the country, including 100 champion truck drivers competing in a National Roadeo of driving skill. These data were supplemented by measurements taken on a large sample of military drivers. Comparable distributions for the general driving population are not available at present.

In Figure 1 the percentile distributions of three body dimensions are given: anterior arm reach, knee height, and sitting eye level height. These are known to be important in regard to the location of the seat and the controls in vehicular equipment. Two of the distributions are also shown graphically.[14]

The data are *not* presented in terms of averages, for the use of average values may account for many defects in vehicle design. The mean should not be employed directly, since, by definition, arrangements for the person of "average size" would be suitable for only 50 per cent of the operators in a normally distributed group. Provision for 90 or 95 per cent, or any other predetermined proportion of potential operators, will require identifying the correct cut-off points. For example, where arm reach for the operation of controls is under consideration, the cut-off point should be well below the average reach. In other situations, due consideration must also be given to the 25 per cent of the drivers whose dimensions exceed the average values, as well as to the 25 per cent whose measurements are below the average.

Many serious errors were observed in regard to human sizing. In several models, for example, only 5 per cent of the drivers could comfortably reach and operate the hand brake. In others, only 60 per cent could be accommodated for knee height between the pedals and the steering wheel. Many of the taller drivers are unable to adjust their sitting position to obtain maximum visibility with regard to their instruments and the road ahead.[15]

Failure to provide for adequate seat adjustment to allow for variations in human size frequently was reported by the drivers interviewed and from the objective studies of working areas. Probably the most striking defect was that the front of the seat could not be lowered for shorter individuals to enable them to operate the pedals without excessive pressure under the knees. Some of the medical problems frequently observed in truck drivers are believed to be related to poor seat design and to failure to provide adequate shock absorbers.[19]

On the basis of static anthropometric data it has been possible to specify dimensions for certain distances and clearances within the driving cab to accommodate the middle 90 per cent of the drivers with respect to body size.[16]

Dynamic Anthropometry and the Use of Mockups

The problem of integrating anthropometric data with the static dimensions of cabs is one of varying complexity. The reason for this is that most body measurements are made under static conditions. On the other hand, if a man is driving he is in a *dynamic situation*. As a result, the static data cannot always be applied without additional study through the use of mockups in connection with subjects representing known

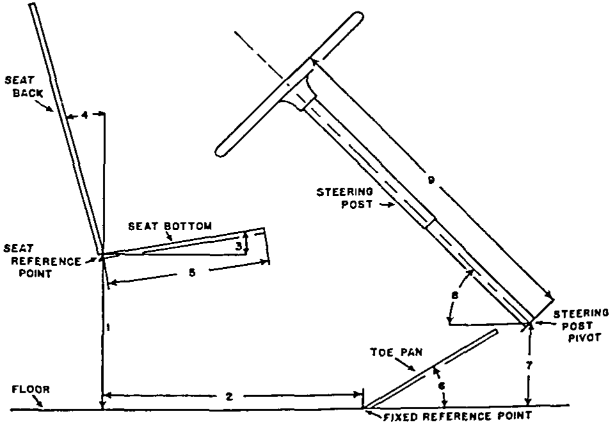


FIG. 2. Shows how the knee of a taller driver is trapped under the steering wheel when the shift lever is in a left position, so that he cannot raise his foot to the brake without first shifting gears. (McFarland & Moseley: Human Factors in Highway Transport Safety, Boston, Harvard School of Public Health)

points in the distribution of body measurements.

Similarly, faulty design may be overlooked without direct observation of the driver operating his equipment For example, when one truck model was evaluated, it was discovered that taller drivers could not operate the foot brake when the gear lever was in either of the two left positions (Fig. 2). It was impossible for a driver to put his foot on the brake pedal without first shifting gears. For 80 per cent of the drivers the distance between the brake pedal and the bottom of

FIG. 3. Schematic diagram of the mockup truck cab. Shows the various adjustments available to the subject and the manner in which each was measured. (cf. McFarland, R. A.: Soc. Automotive Engineers Tr 64:737)



the steering wheel was too short to permit the leg to move high enough to put the foot on the pedal. Furthermore, the gearshift in either of the left positions was too close to the wheel to allow the leg to slip between. As a result, the foot was trapped on the floor until the driver could shift gears.[15]

The principle that static dimensions require supplementary technics involving the dynamic setting of the driver at his task was applied in an additional experiment. The objective was to determine the ranges of adjustability in the seating and controls which would result in optimal accommodations for individual operators. A cab mockup was devised in which 9 different adjustments could be made. This apparatus is shown schematically in Figure 3. Subjects representing the 5th, the 50th and the 95th percentiles of Army drivers "drove" the device in a simulated driving task at various settings of the adjustments. The interrelationships between the various items in the cab were determined by statistical analysis, and recommendations were made for their location and ranges of adjustability. A significant finding of the experiment was that when the settings in the apparatus were those at which the "driver" was most "comfortable," fewer errors were made on the "driving" task.[9]

HUMAN CAPABILITIES AND BIOMECHANICS IN RELATION TO THE DESIGN OF OPERATING CONTROLS

Many errors leading to highway accidents can be prevented if the controls are designed and located so that they can be operated easily, accurately and rapidly. This is especially true in regard to switches and knobs, such as those for headlights, foglights and cigarette lighters, and in regard to foot pedals and shifting levers. Particular attention should be given to the shape and the color coding of knobs, the radius of knobs, the gear ratio and the amount of inertia and friction. These factors become of critical importance at high speeds or in heavy traffic.



FIG. 4. Location of the dimmer switch. The switch button in this model is directly beneath the brake and clutch pedals, and very close to the steering post. (McFarland & Moseley: Human Factors in Highway Transport Safety, Boston, Harvard School of Public Health)

One possibility of reducing errors is through improvement in design to simplify the more complicated operations. Some of the important factors relating to the design and the operation of controls are: (a) their location for ease and accuracy of reaching; (b) the direction of movement for greatest efficiency; (c) the amount of force that must be applied for operation; (d) rate of movement from point to point; (e) speed and amount of rotary or wrist movement required in wheels or knobs; (f) size and shape; (g) frequency of use; and finally (h) the degree to which the control performs a critical function. A considerable amount of data of this nature is currently available and may be applied to problems of automotive design.[3,6,27]

In the automotive field, a serious accident resulted when a driver, while proceeding at high speed in a modern car, inadvertently shut off his headlights in the belief that he was operating the cigar lighter. The knobs for these two were identical in shape and size, and located close to each other on the dashboard.

THE DESIGN OF SWITCHES AND KNOBS

The location and the design of switches and knobs may be the source of errors or accidents, as previously noted. In two trucks, the dimmer switch was found to be

located directly beneath the foot pedals, close to the steering post (Fig. 4). In these models the driver may inadvertently operate the air horn or the foglights while attempting to dim his headlamps. Even when he operates correctly, more complex motions and longer reaction times are required to avoid the pedals. Since many accidents occur when approaching another vehicle, the location of the switch underneath the pedal may cause undue delay in pedal operation. Adequate shape coding for the accurate identification of knobs and switches by feel or touch might be used to great advantage (Fig. 5). Also, greater standardization in the location of switches might aid in the reduction of accidents which are attributed to the inadvertent operation of a wrong control. The use of these principles might have prevented the accident described earlier in this section.

The Design of Foot Pedals and Levers

The various pedal relationships offer a promising area for study and improvement. In some instances the brake and the accelerator pedals are so placed that they force the driver to make lengthy movements in three directions before the brake can be activated, i.e., up, over and then down. Sometimes the two pedals are of identical design and material, making it almost impossible for the driver to distinguish between the pedals by "feel" alone. Undoubtedly this feature has been responsible for many critical situations and probably a certain proportion of real accidents as well, especially with drivers new to a particular vehicle.

Individual muscle groups may become acutely fatigued from holding a steady position, especially if at a cramped angle. The lower right leg and foot, for example, may react slowly in emergency situations after maintaining steady continuous pressure against the accelerator pedal. In some situations, as on runs in mountainous country, continuous turning and shifting are required. Mechanized or hydraulic aids to steering will continue to reduce the possibility of errors during such combined maneuvers.

HUMAN LIMITATIONS IN RELATION TO THE DESIGN OF INSTRUMENTS AND WINDOW AREAS

A driver must receive clear and unambiguous information concerning his automobile and must have an unobstructed view of the surroundings for efficient and safe operation. The driver receives by far the greater part of this information via visual perception; thus an important area of consideration is the visual display.

The Design of Instruments and Displays*

Often a driver spends too much time

* The following factors are important in regard to ease of seeing: (a) size and spacing of critical detail, especially in instrument markings and figures; (b) contrast between object and immediate background, (c) amount of illumination, including the use of color; (d) contrast between the objects to b[illegible] sign criteria for [illegible] numbering of i[illegible]gible width and length of pointers, have been determined experimentally. Figure 6 illustrates a few of these principles [5, 27]

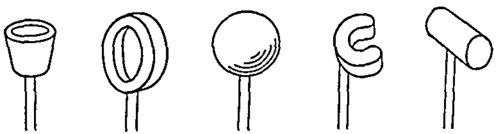


Fig. 5. Shape coding of knobs and handles. Shown are several shapes which can be distinguished easily from each other by touch, without the aid of vision.[3] (After Chapanis, Garner and Morgan: Applied Experimental Psychology—Human Factors in Engineering Design, New York, Wiley)

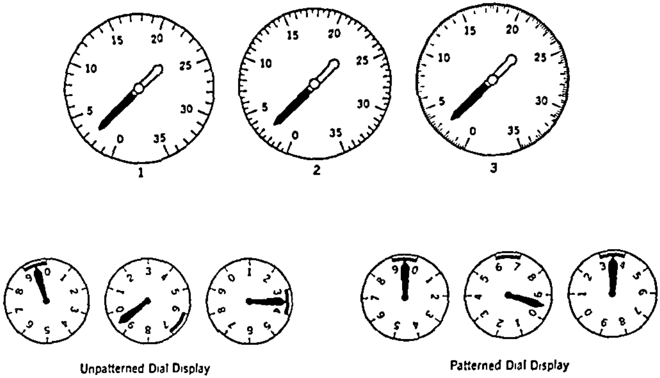


FIG. 6. The design of dials for ease of reading. In the top row of dials, that at the left can be read most quickly and with fewest errors. In the bottom row of dials, detecting the instrument showing a deviation from the normal range is more rapid in the patterned display at the right.[3] (Chapanis, Garner and Morgan: Applied Experimental Psychology—Human Factors in Engineering Design, New York, Wiley)

reading an illegible instrument or looking for a specific switch or instrument among others of the same size, shape and general design. At other times the dials may be behind the steering wheel or too far away to be read easily. All of these items—design, placement and legibility—may seem trivial, in that improvements may result in saving only one tenth of a second, but, at 40 miles an hour, a tenth of a second can well mean the difference between life and death.

Almost all automatic instrumentation is of the numeral, marker, pointer type. This necessitates direct reading of numerical values However, many of the instruments may be more usefully designed for check reading, with normal values indicated by a common position of the pointers, requiring scrutiny only when a marked deviation of pointer position occurs. The nine o'clock position has been shown to be satisfactory for this purpose, since the zero or normal position is at nine o'clock and the needle rises or falls for an increase or a decrease in value.*

DESIGN FOR VISION OF THE ROADWAY AND SURROUNDINGS

The design of windshields, side windows and rear-vision mirrors represents one aspect of the visual display. Studies of operating efficiency and accidents indicate that additional research should be carried out in these areas. Adequate vision from the vehicle remains a serious problem in some auto, bus and truck models, although marked improvements have been made in others.[10]

Man's Area of Vision in Relation to Windshield Design. The range and the field of view for drivers from all types of vehicles is an important area for the applica-

* Although visual displays are more common, auditory signals can also be used if they are recognizable against the general sound background. In such cases an attempt should be made to use a frequency range where the ear is most sensitive and shows least masking by the noise background, or is least subject to hearing changes due to age.

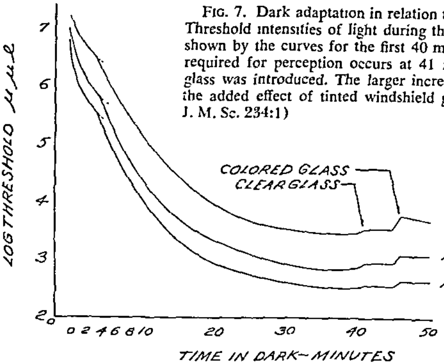


FIG. 7. Dark adaptation in relation to age and the tinted windshield. Threshold intensities of light during the course of dark adaptation are shown by the curves for the first 40 minutes. A slight rise in the light required for perception occurs at 41 minutes, when clear windshield glass was introduced. The larger increase at 46 minutes demonstrates the added effect of tinted windshield glass. (McFarland, R. A.: Am. J. M. Sc. 234:1)

tion of human-engineering research. In a study associated with the Harvard project, methods are being developed for the objective *rating of vehicles of various kinds in* terms of the visibility from the eye position of the driver. An instrument has been devised by King and his associates which permits numerical comparison of the outside physical area visible through various arrangements of windshields, windows and supporting structures with the total area man is capable of viewing. This study is concerned with improving the design provisions for seeing other vehicles and stationary objects *in time to introduce appropriate* action [1] The effect of curvature in the windshield on the accurate perception of the location and the distance of objects represents another factor requiring study.[19]

Visibility Through Tinted Windshields at Low Illumination. There is no better example of the importance of the interrelationships between the operator, his equipment and the environment than the use of tinted windshields on vehicular equipment. *These windshields have been widely* accepted in America, and certain advantages may be obtained in reducing the glare from bright sunlight and aiding in the control of temperature within the car. Since the National Safety Council reports that *accident rates are three times higher at night* than in the daytime, this design feature deserves careful consideration in order to utilize the principle to the greatest advantage without introducing hazards.*

Age is an important consideration in evaluating the significance of these findings. It is now well established that with *increasing age there is a decrease in the* sensitivity to light of the retina under low levels of illumination. The correlation for this relationship in our experiments was found to be .895, one of the highest yet reported between age and a biologic function. *From the data it was calculated that for every increase of 13 years in age, a doubling of the intensity of dim lights and*

* [illegible] mate [illegible] as c[illegible] glass. Carefully controlled tests in the Harvard project indicated that, at low levels of illumination, objects just perceptible without the glass could not be perceived through the tinted windshield unless their brightness was increased by a factor of about 1.45 [19]

*objects would be required for them to be just above the threshold of perception.**[17]

THE CONTROL OF ENVIRONMENTAL FACTORS, INCLUDING DECELERATIVE FORCES

An additional factor influencing the efficiency and the safety of the driver is the physical variables of his environment. These may be broken down into the major areas of temperature, humidity and ventilation, noise, vibration, carbon monoxide and the forces involved in deceleration. Extremes in any of the variables will result in the discomfort and the lowered efficiency of the driver, as well as the discontent of the passengers. For each of these variables there are reasonably well-defined ranges of comfort and discomfort, and extremes which may give rise to accidents.[20]

Temperature, Humidity and Ventilation

A change in any one of these variables will affect the other two insofar as they determine comfort. Hence, all three must be considered as a unit. Composite curves have been developed by the American Society of Heating and Ventilating Engineers to show the various comfort zones and the typical subjective responses to heat, cold and humidity.*[8]

One of the most important requirements for driver and passenger comfort relates to air movement and the amount of fresh air used in ventilating the car. Very low rates of air movement will produce a feeling of stuffiness, and body odors and tobacco smoke may become very irritating. Optimally, from 35 to 40 cfm of fresh air should be supplied per individual at velocities of between 20 and 60 fpm in order to maintain a sense of freshness without creating undesirable drafts. It should be remembered that increased air velocities tend to have a greater cooling effect, which may be advantageous in summer but uncomfortable in winter.

The most important implication of the atmospheric variables, however, is the fact that human performance has been shown to deteriorate significantly at temperatures of about 83° Effective Temperature and above (the equivalent of 83° F. at 100% humidity).[21] Of the different types of skills which show deterioration, many are activities having direct relationships to safe driving. These results were obtained with industrial workers, and the same procedures should be carried out with drivers. Poorly ventilated vehicles undoubtedly give rise to lethargy and sleepiness, and thus contribute to accidents.

Noise

The noise levels in most passenger automobiles are sufficiently low to require few design changes from the point of view of driver health and safety. This is in marked

* When the decrease in light sensitivity of the older eye is combined with the reduced transmission of light by the tinted glass, a serious question of safety during night driving may be raised. Carefully controlled operational studies will be required to determine the practical significance of the findings in this area. At present the results of our laboratory studies indicate that at any age the effect of the tinted glass at night is to reduce the visibility of lights and objects near the threshold of perception, and that though the influence of age is of greater magnitude than that of the glass in reducing visibility, the effect of the glass is relatively greater for older persons. Figure 7 illustrates these findings. The first portion of the curves shows the course of the sensitivity threshold for groups of subjects covering the age range of 16 to 89 years during 40 minutes of dark adaptation. The slight rise in the thresholds at 41 minutes results from the introduction of clear windshield glass, while the substantial rise at 46 minutes follows the viewing of the test lights through tinted windshield glass.[1]

* The optimum range for winter is from 68° F. to 72° F. (dry bulb), and for summer from 74° F. to 78° F. A relative humidity of 30 per cent to 70 per cent is quite acceptable in these zones. Excessively high humidities are uncomfortable at high temperatures and result in feelings of coolness or dampness at low temperatures. When the humidities are below 15 per cent, the membranes of the eyes, the nose and the throat become uncomfortably dry.[13]

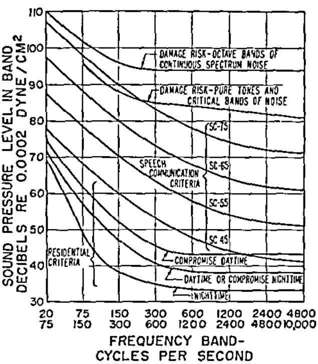


FIG. 8. Criteria for noise control.[23] (Rosenblith, W., *et al.*: Handbook of Acoustic Noise Control, vol. 2, Noise and Man, Dayton, Ohio, Wright Air Development Center)

contrast with the situation of some commercial vehicles.*

An octave band analysis of the noise *outside* heavy and medium trucks made by Callaway revealed heavy trucks to reach a peak of 93 decibels in the 75 to 100 cps frequency band, dropping to 80 decibels in the 600 to 4,800 cps bands. Those taken on a passenger automobile during the same investigation reached a maximum of only 64 decibels in the 150 to 300 cps band.[2] Only in the latter vehicle has a sufficiently low noise level been maintained. The noise from trucks is a serious problem to residents of many communities. The wide range of differences in noise levels from the quietest and the noisiest trucks indicate that some designers at least have been able to make great improvements. Suggested criteria for the designer in this respect are shown in Figure 8.[23]

Vibration

The human body is very sensitive to the various types of vibration encountered in motor vehicles, especially to those in trucks. There is no doubt that excessive vibration leads to discomfort and fatigue in driving operations. Evidence is also accumulating that serious physical disorders may result from protracted exposure to excessive vibration.[24] Under less extreme conditions, visual acuity is affected, and certain reflexes are diminished.[3] The physiologic limits of tolerance to vibration are thus of great importance, and collaborative medical and engineering studies are especially needed on the effects of vibration beyond the limits tolerable for health, safety and efficiency.

The subjective reaction varies with the frequency and the amplitude of the vibration. In general, the higher the frequency, the lower the amplitude must be to maintain a given level of comfort. Also, as frequencies increase, the effect tends to be more localized. With slow frequencies the whole body may be involved. Most of the frequencies encountered in motorized equipment are relatively slow, i.e., 8 cps or less.*[13,14]

Carbon Monoxide

Carbon monoxide poisoning is an ever-

* In seven current truck models which were tested for over-all noise levels *within* the cab by the Harvard research group, it was found that the range was from 48 to 89 decibels with the cab closed and the engine idling. On those models which were road-tested under normal operating conditions the second and third gear noise levels were between 80 and 95 decibels and just below 90 decibels in fourth gear.

* The subjective response to vibration, as determined by several investigations, is shown in Figure 9. Thus, a vibration of 8 cps becomes perceptible at an amplitude of .0008", unpleasant at .009", and is judged intolerable at .06". Similar limits may be read from the chart for any given amplitude and frequency.[12] In general, where one is excessively high the other must be made correspondingly low. Ideally, of course, both amplitude and frequency should be reduced as much as possible.

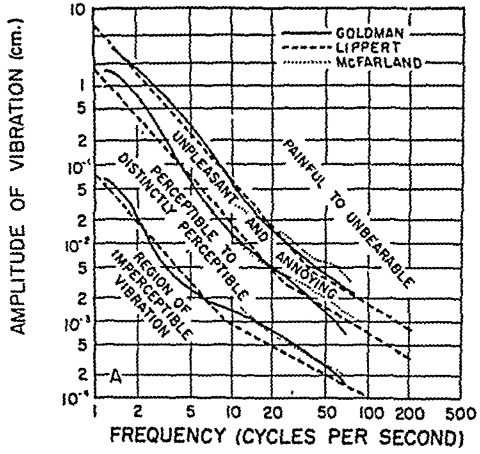


FIG. 9. Subjective responses to vibration. Threshold values for perception, discomfort and tolerance to sinusoidal vibration are plotted from the data of three investigations. (McFarland, R. A.: *Human Factors in Air Transportation—Occupational Health and Safety*, New York, McGraw-Hill)

present possibility in the operation of motor vehicles. The concentration in areas of heavy traffic is being reduced by improved engine, carburetor and muffler design. The problem is becoming increasingly important, however, in relation to smog and heavy deceleration and idling in traffic in metropolitan areas.[7] The influence of carbon monoxide from this source is known to be serious, and it is a health hazard in areas of high traffic density. Also, there are large amounts of hydrocarbons which are discharged into the air from the use, the storage and the transportation of gasoline.

It is well known that small amounts of carbon monoxide will be absorbed rapidly by the blood stream, resulting in an oxygen deficiency which may at first be unnoticed by the individual. The initial reaction of carbon monoxide poisoning consists primarily of lowered attention, difficulty in concentration and retention, slight muscular in-co-ordination, sleepiness and a mental and physical lethargy. These symptoms could easily involve a driver in hazardous situations.[7,12] One of the earliest demonstrable effects of carbon monoxide is to reduce the sensitivity of the eye under low illumination, as in driving at night. For example, chronic cigarette smokers are known to have from 4 to 8 per cent carboxyhemoglobin in their blood, which would correspond in effect to an altitude of about 7,000 feet. If additional amounts are present from the exhaust system of the vehicle, a state of oxygen deficiency having serious implications for safety may result.[12]

In motor vehicles dangerous concentrations of carbon monoxide usually result from leaks in the exhaust system and openings in the floor boards or other parts of the vehicle body. Exposure to even as small a concentration as 0.01 per cent (100 ppm), although having no perceptible effects for several hours, should not be permitted over long periods of time. It is desirable to limit

the amount of carbon monoxide to .003 per cent (30 ppm).*[7,13]

Decelerative Forces

The decelerative forces involved in sudden stops will result in bodily injury to the occupants if they are thrown forward against the windshield, the dashboard or other structures or projections. The degree of safety is dependent in large part upon the rate at which the vehicle stops. Ideally, the brakes of a modern vehicle are capable of producing a deceleration of up to 1 g (32 feet/sec^2), but in practice it has been found that 20 feet/sec^2 is the maximum that can be expected in most circumstances. This figure is considerably higher than those determined for the points at which a person riding in a vehicle feels discomfort or must prepare to avoid bodily injury.

A series of controlled braking stops were made from a speed of 70 mph, and the subjective responses of the drivers and the passengers were recorded. On the basis of the data obtained, the maximum limits of deceleration for comfort can be set slightly below 11 feet/sec^2. However, as these forces approached 14 feet/sec^2, the reaction was judged severe, and the passengers had to prepare to avoid injury.[26] Since high decelerative forces will occur only during conditions of emergency, they cannot be controlled completely through driver choice. The ultimate solution then is to prevent injury to the occupants of the vehicle insofar as is possible once such conditions occur.

Research by Stapp, DeHaven, Dye and others on the ability of the human body to withstand sudden deceleration and impact forces has indicated that the force of many accidents that are now fatal may be within the physiologic limits of survival.[4,22,25]

It was found, for example, that a human being can withstand very high decelerative forces without injury if he is properly restrained. On the other hand, a speed of 15 miles per hour can cause death if the momentum of the head is not checked during rapid deceleration of the vehicle. If a 10-pound object, the approximate weight of a human skull, falls 1 foot and strikes an area 1 inch square, the deformation would be very slight. On the other hand, under the same conditions, if an object 1 centimeter square is struck, a puncture fracture would result.

Controlled research in this area is defining not only the tolerances which the human body can stand but also the variables within a decelerating vehicle which result in injury. This requires a uniform system of obtaining data on the causes of injury *within* automobiles in crashes. At the Automotive Crash Injury Project at Cornell Medical College, case histories are being accumulated at a rate of 8,000 a year, from twelve states.[1] Some of the findings which have resulted from the correlation of injuries with data on the portion of vehicle structure involved are as follows: One or more front doors opened in from 44 to over 50 per cent of the injury-producing accidents. Rolling over of the car significantly increased the frequency with which front doors opened. When front doors opened, one out of four occupants was completely ejected from the car. Complete ejection through opened doors approximately doubled the risk of sustaining moderate through fatal injuries.[22]

Studies of the specific features of vehicular designs that cause injuries in crashes offer considerable promise in reducing fatalities. Obviously, automotive engineers can make a great contribution to reducing these in-

---

* Studies made at the Harvard School of Public Health indicate that air leakage into moving vehicles will often suffice to keep carbon monoxide fumes at a safe level. However, there is some chance that drivers entering closed truck cabs left standing with the engine idling may be affected by the accumulated carbon monoxide.[15] There is also a possibility that drivers who remain in a closed idling cab for more than 15 minutes will be affected by the gas. There have been some cases of drivers found dead at the wheel from carbon monoxide poisoning. Exhaust systems should be made more resistant to the loss or the leakage of fumes, and drivers should be well indoctrinated in the procedures for airing vehicles left standing with idling motors.

juries and fatalities if preventive action can be taken at the source, namely, the vehicle itself. The role of restraining devices also offers a promising field for all those concerned with automobile safety.[1]

In order for the designers of motor vehicles to reduce injuries in future vehicles, it is necessary that they be given data concerning the magnitude of the energy and its rate of absorption which result in definite injury. Physicians especially may make a contribution by helping to define the stress characteristics of the human body and the injury thresholds of its parts. For example, recent research has yielded some quantitative data on the variables involved in two kinds of injuries of the human head, i.e., cerebral concussion and skull fracture.[1]

The Limits of Physical Variables for Driving Comfort and Safety

A schematic interpretation of the various stimuli encountered in driving is given in Figure 10 in terms of limits for comfort, dis-

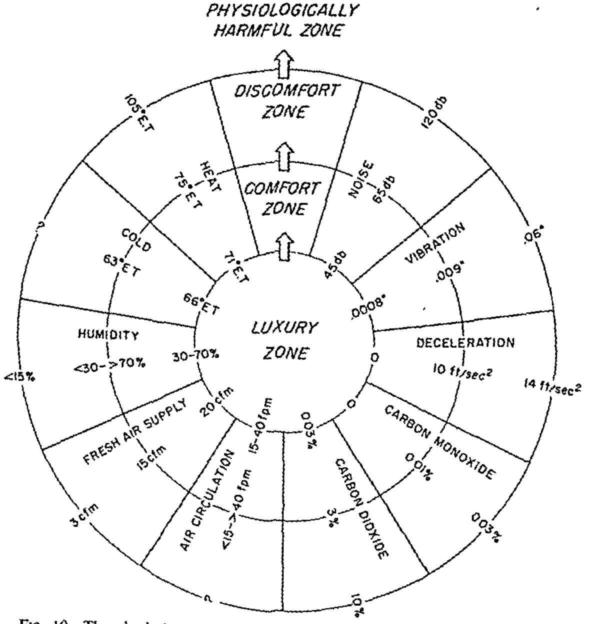


Fig. 10. The physical variables of the environment influencing *driver comfort* and safety. These values must be considered approximations, since each variable is interdependent on one or more additional factors. (McFarland, R. A.: Soc. Automotive Engineers Tr. 64:639)

comfort and physiologically harmful zones.[20] The values indicated in the figure cannot always be considered as rigid standards because of the interdependence of one variable with another. The difficulty of giving a single numerical value as a standard is exemplified in the limits for carbon monoxide. The generally accepted maximum value is 100 ppm of carbon monoxide in circulating air for prolonged exposures. This figure may be satisfactory for a person sitting quietly at sea level, but it should be reduced if the amount of exercise, the degree of ventilation or the length of time increases. The permissible amplitudes for vibration, on the other hand, apply only at frequencies of 8 cps or less. Frequencies higher than this are probably not a major factor in automobile operation. The same complexity characterizes almost every other function that has been discussed.[13] Linear scales or straight-line functions are not so adaptable to the study of human variables as are nomograms, in which one can ascertain the effects of altering any one of the variables upon the others.

SUMMARY AND CONCLUSIONS

1. A new approach has been developed which emphasizes the collaboration between the biologic and the engineering sciences in highway safety. This may be referred to as human engineering or biotechnology. Although it is recognized that most accidents result from human causes, it has been proposed that an additional way of advancing highway safety is to increase the integration of the driver with his vehicle. It was stressed throughout that mechanical design should be based upon the biologic and the psychological characteristics of the drivers, and that vehicles should, therefore, be designed from the man outward with instruments and controls considered as extensions of his nervous system and body appendages.

2. Physicians and surgeons, because of their training and background in the biologic sciences, can make an important contribution to the human engineering team. Although the medical scientist is not responsible for design defects, he can collaborate with automotive engineers in bringing about improvements. Not only can he help in discovering the causes of accidents from this source, but he can aid in preventing them by adequate indoctrination of his patients. Finally, a knowledge of biotechnologic principles may assist the physician in treating highway injuries most effectively.

3. The advance analysis of automotive equipment in the interests of safety was emphasized. Defects in design can be anticipated and avoided before the vehicle is put into production by these methods. This requires (a) an operational job analysis, (b) a functional concept of accidents, (c) an awareness of human limitations and (d) the provision of wide tolerances, or margins of safety.

4. Some general principles were discussed for the arrangement and the design of the driver's working area. These included the use of human body size data to indicate the location and the relationships of seats and the various foot and hand controls, human capabilities in relation to the design features of the controls, and the human factors to be considered in the design of instruments. In general, any control that is difficult to reach or operate, any instrument that is difficult to read, any seat inducing discomfort, or any obstruction to vision may contribute directly or indirectly to decreased driver efficiency and eventually to accidents.

5. Such environmental variables as temperature, humidity, ventilation, noise and vibration were discussed with reference to the comfort, the health and the safety of the driver. Data were presented to show the desirable and the undesirable limits of these factors as an aid to the designers of automotive equipment.

6. Attention was also directed to the fact that the decelerative forces of many fatal accidents theoretically have been within the physiologic limits of survival when the individuals can be given the proper protection.

Current research on relationships between crash injuries and the design of vehicles then was reviewed briefly. Important applications from these studies have already been made in some automobiles.

7. Significant advances in automobile safety can be achieved when the basic physical, physiologic and psychological characteristics of drivers are associated with the specific design characteristics of motor vehicles under given environmental conditions and at particular times and places. Factual information of this type can be discovered only by carefully controlled experimental and clinical studies, epidemiologic surveys and statistical analysis. A dynamic and continuous safety program can produce positive results only by the constant application of the fundamental principles resulting from such studies.

REFERENCES

1. Annual Report of the Commission on Accidental Trauma: Armed Forces Epidemiological Board, Dept. of Defense, Washington, D.C., 1955-1956 and preceding years.
2. Callaway, D. B.: Measurement and evaluation of exhaust noise of over-the-road-trucks, Soc Automotive Engineers Tr. 62: 151-162, 1954.
3. Chapanis, A., Garner, W. R., and Morgan, G. T.: Applied Experimental Psychology—Human Factors in Engineering Design, New York, Wiley, 1949.
4. DeHaven, H.: Accident survival—airplane and passenger automobile, Crash Injury Research Project, N 60NR, 264-12, Cornell Univ Med. Coll., 1952.
5. Fitts, P. M.: Psychological aspects of equipment design, Technical Rep. 5829, Air Material Command, USAF, Wright-Patterson Air Force Base, Dayton, Ohio, 1949.
6. Handbook of Human Engineering Data, ed. 2, Medford, Mass., Tufts College Inst. for Appl Exper. Psychol., 1951.
7. Health, Medical and Drug Factors in Highway Safety: Publication 328, Washington, D.C., National Academy of Sciences, National Research Council, 1954.
8. Heating, Ventilating, Air Conditioning Guide, vol. 22, New York, Am. Soc. Heating & Ventilating Engineers, 1944.
9. Kephart, N. C., and Dunlap, J. W.: Human Factors in the Design of Vehicle Cab Areas, Lafayette, Ind., Occupational Res. Center, Psychology Dept., Purdue Univ., 1955.
10. King, B. S.: Measurements of man for making machinery, Am. J. Phys. Anthropol. 6:341-351, 1948.
11. McFarland, R. A.: Human engineering; a new approach to driver efficiency and transport safety, Soc. Automotive Engineers Proc. 62:335-345, 1954.
12. ———: Human Factors in Air Transportation—Occupational Health and Safety, New York, McGraw-Hill, 1953.
13. ———: Human Factors in Air Transport Design, New York, McGraw-Hill, 1946.
14. McFarland, R. A., *et al.*: Human Body Size and Capabilities in the Design and Operation of Vehicular Equipment, Boston, Harvard School of Public Health, 1953.
15. ———: Human Factors in the Design of Highway Transport Equipment: A Summary Report of Vehicle Evaluation, Boston, Harvard School of Public Health, 1953.
16. McFarland, R. A., Damon, A., and Stoudt, H. W.: The application of human body size data to vehicular design, Special Publication No. 142, Soc. of Automotive Engineers, 1956.
17. McFarland, R. A., and Fisher, M. B.: Alterations in dark adaptation as a function of age, J. Gerontol. 10:424-428, 1955.
18. McFarland, R. A., Moore, R. C., and Warren, A. B.: Human Variables in Motor Vehicle Accidents: A Review of the Literature, Boston, Harvard School of Public Health, 1955.
19. McFarland, R. A., and Moseley, A. L.: Human Factors in Highway Transport Safety, Boston, Harvard School of Public Health, 1954.
20. McFarland, R. A., and Stoudt, H. W.: Physical variables influencing driver comfort, efficiency and safety, Boston, Harvard School of Public Health, 1955.
21. Mackworth, N. H.: Researches on the Measurement of Human Performance, Medical Research Council, Special Report, Ser. No. 268, London, His Majesty's Stat. Off., 1950.
22. Moore, J. O.: Automotive Crash Injury Research, Annual Report 1956-1957, Cornell Medical College, New York, 1957.
23. Rosenblith, W., *et al.*: Handbook of Acoustic Noise Control, vol. 2, Noise and Man,

WADC Technical Report 52-204, Aero-Medical Laboratory, Wright Air Development Center, Wright Patterson Air Force Base, Dayton, Ohio, June, 1953.
24. Simons, A. K.: Tractor ride research, Preprint No. 653, Society of Automotive Engineers, New York, 1951.
25. Stapp, J. P.: Effects of mechanical force on living tissues: I. Abrupt deceleration and windblast, J. Aviation Med. 26:268-288, 1955.
26. Starks, H. J. H.: The factors which influence the braking performance of vehicles, Motor. Ind. Res. Assoc. Bull, second quarter, pp. 17-33, 1950.
27. Woodson, W. E.: Human Engineering Guide for Equipment Designers, Berkeley, Cal., Univ. California Press, 1954.

4
The Need for Motorcar Legislation*

HORACE E. CAMPBELL, M.D.†

We will consider three aspects of the motorcar problem—roads, people, the vehicle itself—and it will be seen that they are the basic factors.

One of the first things to be done about roads is to get more of them. Our motorcar production figures are often a matter of boasting, and yet we have been shortsighted enough to produce more cars than we have roads to accommodate them. In the period 1945 to 1954, 27,600,000 *additional* motor vehicles were put in use on our highways. During the same 10-year period, we constructed 53,000 new "lane miles" of highway. It is estimated that if the motor vehicles put in use during this same period were placed bumper to bumper, they would extend a distance of about 88,900 miles, nearly four times round the globe. In other words, our lane mileage, or added capacity, has been increased only slightly more than one half the total length of the motor vehicles put into use during the last decade.

Doctors must concern themselves both with the lack and the *kinds* of roads that we have. We have all driven round curves where the roadway slanted the "wrong" way and have all cursed the highway engineer who built it that way. (He had a drainage problem to solve and a limited budget. Probably, too, he thought that people drove too fast anyway and that he would do something to slow them down.)

On one of the test tracks in the Detroit area recently, a group representing the American College of Surgeons was given a demonstration of what a safe highway really is. We noted that the car was gaining speed rapidly, all of us noted that the needle passed 80, and then we saw the driver remove his hands from the steering wheel and fold his arms. The car entered a curve, made a 180° turn, entered a straightaway going in exactly the opposite direction, and then the driver placed his hands again on the wheel. This was a demonstration, he said, of power

* Paper read on May 17 during the 88th annual session of the Nebraska State Medical Association under the auspices of the Nebraska Chapter of the American College of Surgeons.

† Denver, Colorado.

(Dr. Campbell's contribution to this symposium was a spontaneous one—and most welcome. It helps to fill a large gap—that of Enforcement—in this part of it, i.e., accident prevention blended with prevention of injuries. Dr. Campbell makes a vigorous appeal for more and wiser laws to ensure greater safety from all three major angles of approach to the problem—the highway, the driver, the vehicle. One deterrent to greater law enforcement all along the line stems in part, I believe, from a failure to realize that law enforcement has been allowed to lag much too far behind education and engineering in regard to traffic safety. An awareness of this certainly will neutralize one's reactions to what otherwise appears to be an undemocratic approach to the problem. It must always be kept in mind that any real progress now has to come from advances on all three fronts—education, engineering, enforcement. None can be subordinated to any one of the others. People like Dr Campbell who are trying to tighten the loose reins of enforcement actually are not as radical as they may appear to be to some of the more conservative readers. They are, the people willing, attempting merely to raise the level of enforcement to meet the advances that have been made in education and engineering. In other words, without the backing of improved laws and their enforcement, all other progress becomes static and will wither and die on the vine even before the benefits promised from them are born. [Ed.])

steering and safe highway construction. Obviously, the road was banked the "right" way. Surgeons must co-operate in a formal way with those leaders who are endeavoring to get safer roads.

Let us next consider the people who drive the vehicles on our highways.

The basic idea of licensing drivers of motor vehicles is to ensure that these people are (1) physically able, (2) morally responsible and (3) mentally capable of performing this potentially dangerous activity.

This means that the right to drive a motorcar is a privilege that must be *earned* by each individual; it is not a God-given right!

It has been shown that young people who have had a course in driver training meet with far fewer accidents than those who have been taught by their parents or some friend, or who have "just learned." We must implement this altogether logical bit of information. I believe that this training should take place in the public schools, even if this will require additional time, money and rooms or even buildings. But, even a tremendous expenditure will be far less costly than our present outlay, which is estimated to be five times our annual loss by fire. I call for legislation requiring that every new applicant for a driver's license present a certificate of *driver education from either the public* school or other approved source.

We now come to the complex and intricate matter of driver examination, which cannot be discussed adequately here. But, first, we all recognize the importance of adequate vision. I shall not go into details. The burden of my remarks in this area is that the members of our profession who specialize in this field must get into the dust and the hurly-burly of practical politics. At safety conferences and meetings of highway groups, the speaker in this field almost always is an optometrist. When any pronouncements are made in the press about drivers and vision, they emanate from an optometrist. There is a significant area of study in regard to adequate rear-vision mirrors, etc., which should challenge our opthalmologic groups. Our profession must retake the lead in the visual testing of drivers and endeavor to develop new and more adequate visual aids in motorcar driving.

We now come to a real "toughie"—the psychological testing of drivers. It has been shown in industry that money can be saved by weeding out the drivers with psychological difficulties. The City of Detroit, at the Psychopathic Clinic attached to the Recorders Court, has shown the wisdom of channeling the repetitive offender through a clinic rather than round the circle again consisting of court, jail and another accident.

The booklet entitled *Accident Facts*, published annually by the National Safety Council, deserves a place in every doctor's library. According to reports from 22 states, in 24 out of 100 fatal accidents a driver or an adult pedestrian had been drinking. Among the drivers involved in fatal accidents for whom the condition was stated, 20 out of 100 had been drinking. The driver's condition was not stated in 24 per cent of the cases, and it is safe to assume that several of these also had been drinking. After all that has been written and said about mixing gasoline and alcohol, and in view of the fact that such a high percentage of drivers in fatal accidents have been drinking, it would *seem that the situation should be reconsidered.*

We must deal more harshly with the drinking driver than is the case at present. That we are so lenient with such people is because the great majority of us—the baker, the doctor and the candlestick maker—drink and drive. I have watched juries in alcohol cases, and their decision "Not Guilty" in the face of flagrant evidence means simply that they said to themselves, "There but for the grace of God go I." But I think we must go farther than that, and deeper than that, and see to it that any drinking driver at the time of his *first* accident, no matter how minor, is compelled by law to undergo a psychological examination.

One of the most important arguments for

a driver training course is that psychological disorders may be discovered there by the teachers and the pupil subjected to remedial courses at that early stage. The psychological screening of all applicants for a driver's license, both new and old, presents some problems, but the medical profession can develop a simple screening device that can be a step in this direction. All this is postulated upon the necessity that license revocation must become much more frequent than is the case at present, and that enforcement of revocation also must be made much more effective. *This can be done if the American people will realize that the Constitution does not guarantee a person the right to drive in face of defects.*

One of the most important aspects of driver examination is the matter of convulsive diseases, particularly epilepsy. It is almost impossible to ascertain the facts. We have tried. But one thing we have learned is that legislation on the subject of epilepsy must be so framed as not to drive the epileptic "underground." The laws of our states all differ, and most of them are bad. We can lay no claim to having solved this in Colorado, but we are trying. The state of Wisconsin has what is generally regarded as the model law. Dr. Edward Schwade, of Milwaukee, has been the recognized leader there.

I come now to what I believe is the most significant factor in our motorcar death and injury problem, i e., the motorcar itself. It is generally believed that the motorcar is very safe because it has been made safer each year. This is untrue from the standpoint of injury potential in accidents. In point of fact, the converse holds. Actually, Cornell has shown that the models for the years 1950 to 1954 are more dangerous than those of 1940 to 1949, and this applies to 1955 as well. *Only this year has any effort been made to design for safety, and this is most rudimentary and is not industrywide.*

Study and analysis of the last few years have revealed that our crash-death and injury problem is largely one of motorcar design and structural quality. Yet over 50 years of motorcar deaths and injuries have resulted in only four specific laws in Colorado, at least, affecting the motor vehicles themselves: those relating to towing chains, safety glass, lights and brakes.

When a car hits a pedestrian, that person's injury is direct and immediate. On the other hand, the crash of a motor vehicle with another car, with a fixed object, or running off the road does not injure personnel primarily. The primary injury is only to the vehicle. The injury to riders is secondary and is due to blows against surfaces not prepared for that event. In other words, the injury can be prevented independently, despite accidents.

Legislation controlling these interior surfaces has been delayed because legislators, while realizing that laws are necessary, have not known exactly what specifications should be made. They have waited all these years for a concrete program from the medical profession (and engineers). We surgeons have been patching up these motor victims for years and never have stopped to analyze the physical situation in a motorcar crash. It is clear now that none but the most severe crashes need result in death or even injury.

As pointed out formerly, when a motorcar changes direction markedly or stops suddenly, the occupants come to grief by striking parts of the car interior or objects by the roadside. The magnitude of this force is something that few of us have understood and is the basic problem in our motorcar death and injury situation. This force can be modified and controlled by engineering changes in the design of our automobiles.

Should this be left to the gradual evolutionary process of business competition, or should it be hurried along by appropriate legislation? It seems to be history that only by a long series of detailed legislative acts can a total safety program be achieved. Laws must specify the sizes and the colors of highway signs and markings, etc. The American College of Surgeons has taken a

positive lead in its resolution of February 19, 1955, and it is to the surgeons in each locality that we must look for leadership. This does not imply that the American College of Surgeons is recommending legislation in this field, because it is not; it hopes to stimulate competition among the various manufacturers in the field of safety. As I survey the last 25 years of automotive history and the scores of suggestions for safety that have been rejected by the motorcar industry, it is clear to me that specific legislation in each state is the only means by which automobiles will be built that can crash without danger to the occupants. What are the specifications that the lawyers and the legislators would expect us as medical men, familiar with the actual facts of trauma, to suggest?

Everyone knows that the instrument panel is the cause of some of the most horrible injuries. These are inflicted by the knobs and other protuberances which, at only 11 miles an hour, can produce a skull fracture Dye, of Cornell, has shown that a human skull can be hurled at a speed of 70 miles an hour against a steel plate without injury if a pad 4 inches deep is interposed. In other words, the padding on the instrument panel, composed of the newer plastic foam, should be at least 2 inches deep and have a backing of metal whose curves are no sharper than a radius of 2 inches. Behind this metal there should be no fixed structure, so that the metal will be able to deform another 2 inches under the more severe impacts. This same depth of plastic padding should be provided over the corner posts, over the windshield frames and back along the roof for a distance of at least 4 feet, for it has been shown that the rear-seat passengers strike the roof in about this area. As newer substances are devised, these depths and thicknesses may change, hence they should not be incorporated into law. The specific wording in the legislation should be, "embodying structures and surfaces which may yield to a sufficient extent that the human skull may be decelerated from a speed of 65 miles an hour (or other current maximum speed limit) to zero without injury."

Obviously, it is impossible to make the basic structure of the windshield frame with corner posts that will yield on impact; therefore, measures should be taken to keep people from striking these structures at all. Some form of restraining device, which may take the form of a bar extending from the door of the car, or a shelf that may be pulled toward the passenger after he is seated, or the current seat belt, must be provided. Actual mechanical details should not be specified in laws, but the specific measure, i.e., "personnel restraint," or "passenger stabilizing device," should be insisted upon and the degree of restraint specified, i.e., "a minimum of 4,000 pounds." This figure may be changed as time goes on; for example, for a long time aviation belts were officially 2,000 pound belts; later they were raised to 3,000 pounds; and further changes probably will be made as aviation safety progresses. There is every evidence that motorcar belts should exceed aviation belts and have a minimum strength of 4,000 pounds.

One of the most important details of motorcar safety is the need for doors that will stay shut on impact. This year most manufacturers are providing safety door locks. They are of uneven quality, but some are very good In order to get uniform protection, we must have laws governing this detail of construction. I think that this protection should operate at all speeds specified as legal within the state, hence the law should read something like this: "The doors of all motor vehicles sold as new within the borders of the State of Nebraska after July 1, 1957, shall remain closed upon impact of the automobile with a standard concrete and steel barrier at all speeds up to and including 65 miles per hour. The construction shall be such that after said impacts the doors may be opened from within or without with no more than a 100-pound force."

One of the many lessons that those crazy kids, the stock-car racers, have taught us is that car roofs are no good. These clear-eyed realists wire the doors shut and install roll bars. In these days of the so-called hard-top, which looks flimsy to me, we need legislation here if anywhere. "All passenger vehicles with metal tops sold as new within the borders of the State of Nebraska on and after the date of July 1, 1957, shall be so constructed that the automobile may be dropped upon its top from a height of 15 feet upon solid concrete with no more than 4 inches reduction in the height of the roof." A fall of 15 feet equals a speed of about 20 miles per hour, which should represent a modest requirement for roof structure.

Part of the function of the seat belt in today's cars is to hold the seat down. The construction of the adjusting mechanism is so flimsy that even in a modest crash the seat tears loose from its moorings and adds its weight to the blow that the passenger must sustain against the instrument panel and the windshield. With the use of the seat belt, the efficiency of the belt is reduced by the amount of strength required to hold the seat in place, and the motorist is squeezed between the belt and the seat. Let the law state, "All seats and cushions shall be so constructed that they remain in place without displacement or distortion under stress of 20 g forward, laterally and upward."

The steering wheel and the column long have been recognized as a serious source of injury to driver and passengers alike. The manufacturers make the ornament over the head of the steering column in the form of cookie cutters, etc., and one manufacturer brings this ornament to a sharp point. This danger was pointed out to the Vehicle Safety Engineer of that group when the first 1955 models appeared, with the expectation that doubtless it would be changed in the 1956 models. Instead, the configuration is exactly the same in the current model. Cornell pointed out in a report dated March, 1955, that the significantly greater number of deaths and injuries produced by the 1950 to 1954 cars was due to the steering-wheel assembly, and even though bumpers, grilles and taillights were changed in 1956, the steering-column ornament still is sharp and elevated, a rib spreader if ever there was one.

It will require laws—laws with teeth in them—to make manufacturers correct defects of this kind in their products. Happily, one of the larger and more responsible manufacturers has recognized the danger of the traditional steering-wheel assembly and has sought to correct this in the 1956 models. It is difficult to say how the law to deal with this factor should be phrased; I will not attempt it here; but it needs doing.

Another important aspect of motor-car safety is periodic vehicle inspection. All sorts of methods have been tried and are in operation today. There are city-operated vehicle inspection stations in Vancouver, Des Moines, Memphis and elsewhere. There is only one state-wide, state-operated system, I believe, in New Jersey. I have studied material from New Jersey and from Vancouver.

One thing is apparent: an adequate examination will not be made by filling stations and small garages.

Larger garages with heavy and expensive equipment will not make an adequate inspection for the usual fee allowed. Vancouver provides an excellent examination twice a year for 2 dollars a year. Using filling stations and garages, the people in New York State would have to pay 25 million dollars a year, equal to an extra 1 cent a gallon tax to get an examination that the Governor of that state feels is inadequate. At any rate, his fact-finding commission stated that New Jersey had 4.1 defective vehicles among all those involved in fatal accidents, and New York, with no examination system, only 1.7 per cent. An impartial student of the affair must conclude that New Jersey found defects that New York overlooked.

I believe that, since vehicle inspection is

essentially a police function, it must be managed by the authorities. In Colorado, the very people whose cars need inspection find ways of nullifying it.

One suggestion that has been made is that cars up to 3 years of age be absolved from inspection. These new cars in the hands of original owners should not be forced to assume costs of an inspection that they do not need and that properly should be borne by the cars that need inspection.

Whatever mode of administration is decided upon, my study of the matter indicates that big, heavy inspection machines are needed plus a mode of administration with no loopholes.

It is all very well to say, "Let there be a law," but to get one enacted is another thing. The minute it becomes apparent that something is afoot regarding the motorcar, the automobile manufacturers fly their agents in. These men are suave, friendly, very wise, and one must not think that they do not have power. It is not an accident that we have many laws about roads and drivers but very few about motorcars.

Finally, when you find the going tough, recollect the annual death and injury toll that you are trying to ameliorate, that doctors drive automobiles too, and that the lack of crash padding and an energy-absorbing steering wheel may become an intensely personal affair. Therefore, install belts in your car, and in your wife's car, and see that they are fastened every time before the engine is started.

5

Medical Driver Screening: The Fourth "E" of Motor-Vehicle Accident Prevention*

JACOB KULOWSKI, M.D.

The acceptableness of medical screening for driver licensure may be deduced from the oft-repeated query, "Doctor, is it all right for me to drive my car?" This is the keystone of a naturally evolved doctor-driver relationship in regard to physical fitness for the safe driving task. However, in addition to physical fitness, there is the inference in regard to mental, moral, and psychological fitness. Furthermore, it involves a faith in the physician's willingness and ability to pass unbiased judgment on a question the negative answer to which must be accepted, although there is no law to enforce it. Thus, willingly or unwillingly, physicians everywhere have been furnishing the most effective self-imposed deterrents to bad driving that exist today. But, for the most part, this has been a haphazard, unorganized and unofficial kind of responsibility. It has been a "do-it-yourself" way of resolving a duty. Now the press of accident events demands that such a method give way to a "do-it-together" plan of medical action. Can this be achieved in face of the paucity of valid data that relate physical (and other) disabilities, diseases and defects to accidents? Can a beginning be made in this direction? If so, where, and who is to initiate this program? What medical conditions are involved? The answer to the last query is being answered in part by Brandaleone. I shall endeavor to consider the others.

Admittedly, there are few or no available valid data that definitely relate physical disabilities to accidents. As a matter of fact, such data as there are tend to prove that

TABLE 2. ACCIDENT RECORDS OF 31 PARAPLEGICS

	Before	*After*
No. accidents	5	10
No. killed	0	0
No. injured	2	0
Legal responsibility	2	1

25 used automatic shifts; the rest, the conventional type. 9 had had no previous driving experience. Average driving experience was 5 years or 60,000 miles. *Before* and *After* refer to onset of disability. These records compared favorably with people with no disabilities. 24 had restricted permits (with signs attached to plates indicating that the car was hand controlled). Restrictions limited speeds to 40 mph. 90 per cent passed the driver tests required by law of all handicapped persons (Quebec). 10 per cent were not examined. (After Ward and Gingras: Canad. Serv. M. J. 12:459, 1956)

* The author owes data referable to medical standards to Glenn V. Carmichael, Assistant Director, Training Division, The Traffic Institute, Northwestern University, who was kind enough to supply that information in a personal communication dated March 21, 1956.

TABLE 3. ACCIDENT RECORDS IN 70 AMPUTEES (26 ACCIDENTS—17 DRIVERS)

	Minor	*Major*
Legal responsibility	5	2
Not responsible	15	3
Responsibility in question	1	0
No. injuries	0	0
No. deaths	0	1

Calculations were made and compared with the over-all figures of normal drivers in the same areas. The above were not over those of normal drivers. Average number of years of driving was 10 years. (After Shannon: Canad. Serv. M. J. 12:464, 1956)

such afflictions do not result in greater-than-chance number of accidents (Tables 2 and 3). Since the comparison is made with the general driving population—among whom are some who ultimately will be restricted and/or eliminated from this privilege—these data are no more valid than statements based on intuitive thinking. Stated another way, if the general driving population can do no better than amputees or paraplegics, then surely, if for no other reason than this, a closer psychosomatic screening is indicated. Be that as it may, clinical and other experiences in fact point to this requirement. Who is to achieve it?

The start must come from county medical societies, where both general practitioners and specialists can lend a hand (Fig. 11). This program is basic and will need the wholehearted support and co-operation of the public, as well as the sponsorship by county medical societies and individual physicians. *Without medical elucidation and* support, progress in driver licensing will be haphazard, and refinements, however desirable, will not be uniform or lasting. Public support will be sought through properly prepared propaganda by every means of communication (to be paid for by interested commercial carriers and other industries). Medical groups and individual doctors are the only types of citizens who can handle this tricky issue without political repercussions. In my opinion, civic groups will welcome such cultural and intelligent intervention by doctors.

As a beginning, and more specifically, we can do the following to aid official licensing agencies:

1. Caution a patient under treatment when such treatment includes medicine or other therapy that may temporarily affect his ability as a driver.
2. Assist in the training program for examiners, furnishing lecturers in order to improve the training afforded them.
3. When the patient authorizes the giving of information to constituted authority (licensing) for determination of driving privilege, assist the special examiner in arriving at a sound conclusion as to whether or not the driver will be a safe risk on the highway.

However, the epidemic number of accidents, injuries and deaths demand something more in the way of medical screening as an aid in bringing these events under better control.

WHAT HAS BEEN DONE: AREAS TO BE EXPLORED AND DEVELOPED

In general, the following standards quoted from the Uniform Vehicle Code are applicable throughout the various states regarding medical standards for drivers:

> The department shall not issue any license hereunder
>
> To any person who has previously been adjudged to be afflicted with or suffering from any mental disorder or disease and who has not at the time of application been restored to competency by the methods provided by law;
>
> To any person when the commissioner has good reason to believe that such person by reason of physical disability (physical or mental) would not be able to operate a motor vehicle safely upon the highways

The American Association of Motor Vehicle Administrators recommends that persons who are not physically or mentally capable of operating a motor vehicle safely be not licensed.

Almost without exception, states do not license persons who have been adjudged in-

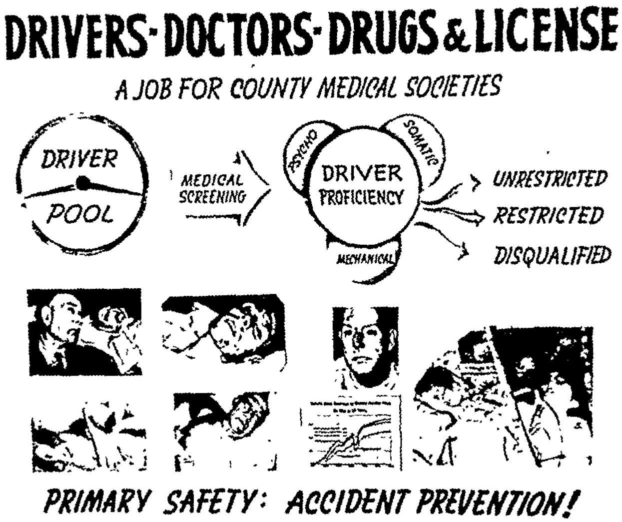


FIGURE 11

sane and have not been restored to competency. Considerable variations exist in the handling of persons suffering from mental disorders, not adjudged insane, who have found it necessary to enter institutions for treatment. Also, institutions discharge many arrested cases because of crowded conditions —a definite problem to driver license administrators because the status of these patients is not clearly defined by the institutions.

Moreover, there are many people suffering from mental disorders who are operating motor vehicles, but *there is not enough evidence to establish that there is a correlation between mental disorders and traffic accidents and violations.* Further research is needed here before definite restrictions or disqualifications can be made on the basis of this element of human personality as it is related to motor-vehicle driving.

Epilepsy has presented all driver license administrators with grave problems. Applicants for driver licenses who admit that they are suffering from epilepsy are not granted the driving privilege unless they can establish that they are under treatment and have been without seizures for some time. There are variations in practice. Some states do not license the applicant if he admits to being so afflicted. Others license if the applicant presents medical statetments to the fact that he can drive safely. The better practices followed by several states require evidence that the applicant has responded to treatment, is continuing under treatment and has not had seizures for periods of time varying from 1 to 3 years. The best studies

and practices have been developed in California and Wisconsin. From evidence developed in California, it appears that freedom from epileptic seizures for 3 years under treatment can be accepted as evidence that a seizure will not occur if medical treatment is continued. The Special Committee on Epilepsy Legislation of the American League Against Epilepsy recommends a seizure-free period of 1 year for a controlled epileptic for him to receive the driving privilege.

The general standard for physical condition, except visual efficiency, requires that the person be of such physical condition that he can control a motor vehicle with safety. The driver must have sufficient strength to control the vehicle: turn the steering wheel and apply the brakes sufficiently to slide the wheels (Fig. 12). He must be able to reach all controls required in the operation of the vehicle, whether by mechanical means on the vehicle or by suitable prosthetic devices.

If drivers with physical deficiencies apply for the driving privilege, they are required to demonstrate successfully that they can operate a motor vehicle. If mechanical or prosthetic devices are needed, the driver is limited to the use of these devices while driving by suitable restriction on his driver's license.

Many unusual cases with handicaps have been noted, and are probably familiar to readers of this chapter. This attests to the need for the highest type of individualization in the proper evaluation of applicants for driver permits. In Wisconsin, a man was licensed even though he had been born without arms: he demonstrated successfully that he could operate a motor vehicle safely with his bare feet. Not long ago the newspapers

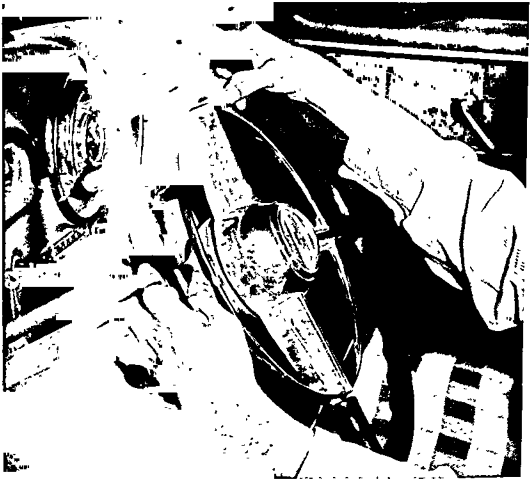


FIG 12 Should this man be granted the driving privilege? He has a good driver record but does little or no driving in the city

reported a high-speed violation by such a driver.

Deficiencies in hearing do not present problems, and drivers so afflicted are restricted merely to an outside mirror on the car that they operate. On the other hand, some deficiencies in other senses—for example, feeling (tactile, heat and kinesthetic)—could cause difficulties in driving if the condition were well advanced. A severe loss of kinesthetic sense could be very critical in driving, but, since this is true, such people are not found on the highways; actually, they are seldom found walking because of the locomotor difficulties involved.

The function of vision in regard to driver proficiency has been given more consideration—and rightly so—than any other element of human physiology in the solution of the driver problem. Almost every state gives some kind of vision test, visual acuity getting more attention than any other aspect of visual efficiency. Although many other phases of visual physiology (and psychology) have been pointed out as essential to safe driving, none has been correlated with accident experience. It is realized, of course, that there must be some visual acuity if the driver is to negotiate his vehicle safely in traffic.

The American Association of Motor Vehicle Administrators and the American Optometric Association recommend a minimum visual acuity of 20/40 (Snellen rating) for general driving, with or without glasses. However, states vary from 20/30 to 20/70, with or without glasses, as the minimum visual acuity standard. Some states will not license any driver whose vision is worse than 20/70, while others will take under consideration cases as bad as 20/200 and license with highly specific restrictions if the driver can establish the need to drive.

Standards for other elements of visual efficiency have not been established, or they are very general in nature. Many states test for color perception, binocular distance perception and field of vision, but still license the deficient driver because there is no evidence that such deficiencies cause traffic accidents. If such drivers can demonstrate successfully that they can distinguish traffic lights, pass other vehicles safely or otherwise compensate for their deficiencies, they are granted the driving privilege and asked to exercise care while driving.

Although night blindness, glare recovery, glare resistance and muscular imbalance and suppression are critical, no standards have been established, and very few states test for these elements of visual efficiency. Naturally, when these functions are gravely depressed the driver will be found rarely on the highways. Thus, for example, marked degree of night blindness would keep the driver off the road at night because he could not compensate for this defect.

Oddly enough, almost nothing has been done in the domain of heart conditions, diabetes, alcoholism, drug addiction, cerebral arteriosclerosis, catalepsy, encephalitis, Parkinson's disease and similar afflictions in regard to driver licensure. However, if evidence is received that a driver is suffering from a disease that affects his driving ability, most states require a driving test to determine how well that person drives and a medical statement from a physician regarding his physical condition.

No state requires a physical examination of its drivers prior to licensing unless there is evidence (definite) of a disease that might interfere with safe driving.

OBSTACLES TO BE OVERCOME

Better licensing control is not forthcoming largely (in addition to lack of medical support) because of the lack of carefully selected trained and well-supervised examiners and driver-improvement officers in adequate number to meet the demands of an increasing driver population.

In contrast with this situation, the fundamentals of driver license examinations are well known. But many items of physical condition are not checked at the examining

station because the tests would be too involved and time consuming, or a definite correlation between the element of personality and the driving task has not been established. Therefore, when cases get too involved, they are sent to a physician for diagnosis and prognosis. This calls for better orientation for clinicians in this regard, since more and more such cases will be referred to them as the examiner load increases. This, also, can best be done at the county medical society level.

One problem currently facing examiners—and one to be reckoned with by physicians in due time—is the finding of adequate time for testing and medical examinations. The former can do little good when the examiner load allows only 20 minutes of examiner time for each applicant. The problem will resolve itself for doctors on two counts: first, family physicians must be given key positions in the examining program but must be well indoctrinated in regard to this vital function; secondly, it is to be hoped that more effective screening will cut down the number of accidental injuries to the point at

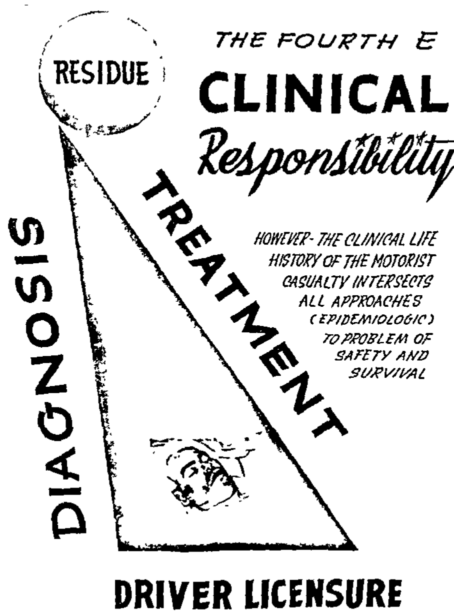


Figure 13

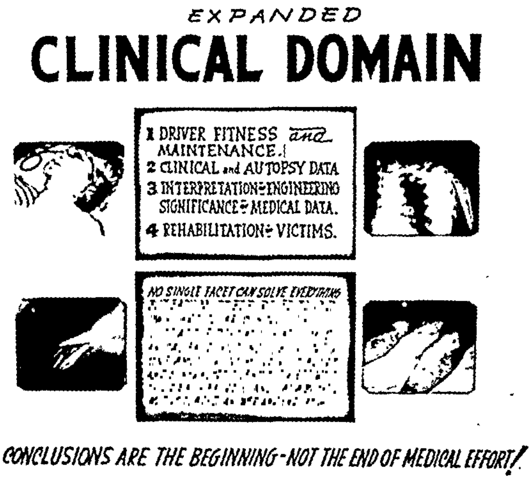


FIGURE 14

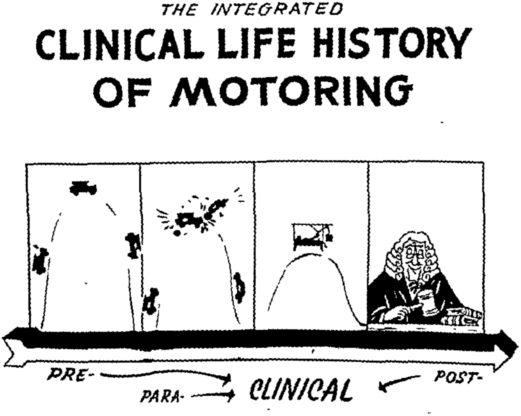


FIGURE 15

which clinicians now burdened with the care of crash victims will have more time to devote to the prevention of accidents and injuries through participation in community-wide programs of medical screening.

SUMMARY

Medical standards for driver licensure have been established only in a general way and vary widely from state to state. If the physician's report indicates that the condition in question is not progressive and that the person ought to be able to drive a motor vehicle, he generally is licensed with suitable restrictions if he can demonstrate successfully that he can operate a motor vehicle safely.

CONCLUDING OPINIONS

Does the expansion of our clinical borders to include medical screening of motor-vehicle drivers as an aid in preventing traffic accidents mean new frontiers in medicine? It does, but only in a strictly narrow clinical sense Epidemiologists, who, after all, are just another brand of individual and collective medical practitioners, paved the way for us some years ago when they conquered other grave threats to our individual and public health and safety. From that standpoint, the modern clinical life history of motoring blurs into the psychosomatic-mechanical factors that govern the preclinical and the postclinical phases of it (Fig 15). Be that as it may, a four-dimensional medical approach to the problem of motorist accidents and motorist injuries promises to fulfill an important niche in the fight for safety which the National Safety Council, along with its subsidiary branches and other affiliated individuals and groups, has waged for so many years. Thus, the etiology and the pathology of motorist accidents and injuries—in the broadest meaning of the words—are being brought into sharper and proper focus with aids to recovery and ultimate rehabilitation of crash victims.

BIBLIOGRAPHY

Kulowski, Jacob: A call to and guide for driver medical screening, Bull. Buchannan County M. Soc., October, 1956.

Shannon, J. G.: Amputees and driving, Canad. Serv. M. J. 12:464-467, 1956.

Ward, H I., and Gingras, G.: Medical aspects of traffic accidents in paraplegics, Canad. M. J. 12:459-463, 1956.

6

Medical Aspects of Motor-Vehicle Accident-Prevention. Study of the Driver

HAROLD BRANDALEONE, M.D., F.A.C.P.*

The importance of motor-vehicle accident prevention is obvious when we realize that in 1954 there were 36,000 motor-vehicle deaths and 1,250,000 disabling injuries as a result of motor-vehicle accidents at a cost of $4,400,000,000.[1]

* Medical Director, Third Avenue Transit System, and United Parcel Service, New York City. The author is indebted to Dr. Gerald J. Friedman, Assistant Medical Director of Third Avenue Transit System and United Parcel Service, and to Edward Flamm, Research Assistant to the Executive Director of Third Avenue Transit System, for their assistance in this work.

(How large a stake industry has in primary and secondary motorist safety may be readily appreciated from a study of this admirable contribution to this [illegible] one, an internist, [illegible] the potential in- [illegible] practice toward the solution of many of the medical problems with regard to motor-vehicle safety that await solution. He has worked over the years to that end and has [illegible] reduce the accident rate on our highways. Moreover, Dr. Brandaleone supports—at least indirectly—this editor's plea for greater participation by industry in the indoctrination of the public regarding voluntary medical screening for driver licensure [and maintenance]. This seems to be the only rational approach to this phase of motoring safety and would serve to engender full-scale participation of the driving population. More important than that, such a program ultimately would enlist the interest and the efforts of family doctors—the veritable medical grass roots of the project It is the hope of the editor that this article will stimulate medical readers to make similar studies in order that the full impact of Dr. Brandaleone's work will be felt in legislative and licensing quarters [Ed])

The human element, the major factor in the cause of motor-vehicle accidents, needs the attention of the medical profession. The National Safety Council reported in 1955 that 1 out of every 14 drivers involved in fatal accidents had a physical condition that could have contributed to the accident. According to reports from 22 states, lack of sleep and fatigue were present in 60 per cent of the cases, with defective vision, illness and defective hearing next in that order.

In 1954 the Industrial Medical Association established a Committee on Standards for Vehicle Drivers.[2] The purpose of this committee was to create medical standards for drivers of all types of motor vehicles. It was the hope of the committee that its recommendations would be used as a guide to physicians, industry and safety organizations in driver evaluation. This committee divided motor vehicle drivers into 3 categories and made recommendations. The categories were:

1. Transportation vehicle operators (bus, trolley, taxi and railroad engineers)
2. Commercial vehicle operators (carrying no passengers, such as trucks)
3. Private vehicle operators

Recently the New York University-Bellevue Medical Center and the Center for Safety Education sponsored a symposium that recommended an interim list of criteria for motor-vehicle operators, but stressed the need for basic research [13] The Massachu-

setts Motor Vehicle Bureau has established a practical method of licensing disabled persons: this plan allows temporary licenses for 3 months with re-examinations by qualified specialists. The Medical Society of the State of New York is co-operating with the State Department of Health and the Motor Vehicle Bureau in developing standards for drivers. The American Medical Association has appointed a "Committee on Medical Aspects of Auto Crash Injuries," under the chairmanship of Dr. Fletcher Woodward, to study this complex problem and to disseminate education to the laity and physicians. Special studies are being performed by highly trained specialists like Dr. Ross A. McFarland, of the Harvard School of Public Health, and, Dr. Herbert S. Gaskill, at the University of Colorado Medical Center.

The importance of the physician to motor-vehicle accident prevention can be seen from the results obtained in the studies of the Medical Department of the Third Avenue Transit System, New York City. In 1947, when we were asked to reorganize the medical department of this company, they had a very high accident rate that had to be reduced. We decided that the best approach to the problem lay in the medical (and other) screening of the operator, with particular stress on the medical and the mental problems involved This required 3 major steps:

1. The establishment of rigid preplacement examinations as part of an improved driver selection program
2. The institution of periodic medical examinations of operators
3. The creation of a comprehensive medical program for employees.

These procedures reduced the accident rate over 50 per cent!

Prior to medical screening, under the improved selection plan of our company, the candidate for the position of bus operator also is interviewed in great detail by the Personnel Department. His previous employment record is investigated. Police files and military medical records are requested. Military records are invaluable in determining the physical and the emotional status of the applicant.

Then the applicant is required to take the American Transit Association motorability tests,[9,10] as well as a group of vision tests on the Keystone telebinocular. He is also examined for glare resistance, peripheral vision and color blindness. Following that the candidate is given a group of psychological tests. If the candidate passes the psychological tests, he is referred to the physician, who takes a detailed medical history, and mental and physical examinations are performed. A roentgenogram of the chest, a urinalysis, serology and electrocardiograms are obtained.

When the examinations are completed and the military records received, the reports are studied by the Medical Director, and the employability of the candidate is determined. We have established a list of minimal physical requirements for candidates and record the findings according to a profile system.[5] The profile (Table 4) is based on a system used in World War II by the Air Force. It includes a physical and a mental examination, and is divided into 6 categories Each category is subdivided into 4 classifications: (1) representing the highest and (4) the lowest grade in each category. A grade of (4) in any group disqualifies a candidate. A grade of (3) in two or more categories may cause rejection.

Briefly, we reject any candidate who might present a disability that would suddenly incapacitate him and be the direct cause of an accident. However, we also disqualify candidates for conditions that may be indirectly incapacitating. For example, severe hemorrhoids may cause a bus operator so much discomfort that his attention may be diverted and cause him to be involved in an accident. A candidate for the job of a commercial vehicle or truck driver who has tuberculosis or a severe low back syndrome should not be qualified for the job if he is required to do heavy lifting. In industry, a thorough

knowledge of job requirement is necessary in order to evaluate the candidate properly. *Our experience has shown that usually 35 per cent of the candidates fail to qualify.* When, finally, the candidate is accepted, he is put through a rigid training program.

In addition to periodic examinations, whenever an employee is absent for more than 28 days because of illness or injury, he must submit to a detailed medical examination to determine his ability to drive safely.

The development of a comprehensive medical service includes the study of absence due to illness. When a bus driver is absent for more than 5 days due to illness, a staff physician is sent to his home to determine the cause of his absence. *There is no interference with the care of his family physician.* The purpose is to determine if the employee is suffering from an illness that would disqualify him as a driver, either temporarily or permanently. In addition, reports are requested from the family physician. The importance of this procedure can be determined from a summary of the following case:

A 48-year-old male, who had been employed as a bus operator in our company, was absent from work for 6 days. His physician certified that he had been suffering from a gastrointestinal upset and that he was able to return to regular work as a bus operator. A staff physician, however, obtained a history indicating that the patient had suffered a convulsive seizure. On this basis he was not permitted to return to work, but a neurologic consultation, including an electroencephalogram, was obtained. These tests revealed evidence of a convulsive disorder associated with hypertensive encephalopathy On the basis of the reports, the operator was not permitted to drive a bus and other work was secured for him He has since had several seizures while at work. This employee has been most grateful that he was not permitted to drive a bus and that he was given a safer job.

PSYCHOLOGICAL TESTING

In an effort to evaluate the effect of psychological testing on the accident rate of bus operators,[4] we employed the Thurstone Temperament Schedule,[14] the Maslow Security and Insecurity Tests[12] and the standard examination for employees recommended by the American Transit Association,[15] all of which are standard procedures. The results of their use have been reported elsewhere.

It is our opinion that psychological testing in general can be an important tool in the selection of the vehicle operator. From our present knowledge it is not likely that any simple screening test will inform us of the emotional characteristics which would make a driver an accident repeater. It is likely that many hours of testing and interviewing would indicate those persons likely to be involved in numerous accidents. But this method is not practical. At the present it is useful for research to determine which characteristics are most likely part of the emotional pattern of the driver with repeated accidents. As a result of this research it may be that simple practical tests will become available for industry and licensing bureaus. However, the beneficial effect of the psychological tests as part of our Selection Program was made evident in 1954 when our company hired 178 new operators. These operators were divided into 5 categories.

The criterion of evaluation is the frequency of accidents per man per month by groups (A/M/M). This was computed by dividing the number of accidents by the number of monthly periods.

Data concerning the length of employment and the number of accidents for each of the 178 operators were obtained from the company's safety department. This information was prepared for IBM analysis to determine the accident frequency per month for each group.

Group 1 contained 3 candidates who were not required to take any tests. This group had an accident rate of .609 accidents per man per month, the highest in the study.

Group 2 consisted of 24 candidates who failed the motorability test and did not take

TABLE 4. THIRD AVENUE TRANSIT SYSTEM

MEDICAL DEPARTMENT

PROFILE CLASSIFICATION

PROFILE CLASS	—P— PHYSICAL CAPACITY OR STAMINA	—O— ORGANIC DEFECTS	—H— HEARING — EARS
1	Able to perform maximum sustained effort over extremely long periods		Auditory acuity: soft whisper audible each ear at 2 feet Audiometric: 0-20-decibels loss Organic defect: none
2	Able to perform sustained effort over long periods	SEE DETAILED LIST OF	Auditory acuity: loud whisper audible each ear at 2 feet Audiometric: 25-35 decibel loss Organic defect: no active or progressive organic disease
3	Able to perform sustained effort for moderate periods	ORGANIC DEFECTS.[8]	*Auditory acuity: normal spoken voice* audible each ear at 2 feet Audiometric: 40-50 decibel loss Organic defect: acute nonprogressive organic disease
4	Below minimum standards for employment		Auditory acuity: loud voice audible each ear at 2 feet Audiometric: above 50 decibel loss Organic defect: Acute or chronic suppurative otitis media Perforation of membrana tympani Severe fungus or other severe chronic infection of the external auditory canal *Chronic mastoiditis*
FACTORS TO BE CONSIDERED	Age, build, strength, stamina, height, weight, agility, energy, muscular co-ordination and functions	Severity in relation to job	Auditory acuity and organic defects of the ears

PROFILE RATING

— E — VISION — EYES	— N — NEUROPSYCHIATRIC	— D — MOTORABILITY GRADE
Visual acuity: 20/20 in each eye uncorrected Organic defect: none	No psychiatric disorder	91 — 100
Visual acuity: 20/40 correctable to 20/30 in each eye 20/100 in one eye correctable to 20/30 (Provided defective vision is not due to active or progressive organic disease) Organic defect: mild superficial infection of lids	Mild transient psychoneurotic reaction Mild character and behavior disorders Borderline mental deficiency	71 — 90
Visual acuity: 20/40 not correctable 20/100 in one eye plus 20/50 in other, both eyes correctable to 20/40 (Provided defective vision is not due to active or progressive organic disease) Organic defect: Astigmatism or muscle imbalance correctable	Mild chronic psychoneuroses Moderate transient psychoneurotic reaction Mental deficiency, mild degree	65 — 70
Visual acuity: below above standards Organic defect: Any severe active or chronic progressive disease of the eye Marked muscle imbalance and/or astigmatism Marked nystagmus Diplopia Impaired depth perception, glare resistance or peripheral vision Severe *color blindness*	Psychosis Moderate severe chronic psychoneuroses Severe transient psychoneuroses (situational) Marked degrees of character and behavior disorders Marked mental deficiency	Less than 65
Visual acuity and organic defects of eyes and lids Special vision tests: Telebinocular Depth perception Glare resistance Peripheral vision Color blind tests—Ishihara	Type, severity and duration of the psychiatric symptoms or disorder existing at the time the profile is determined Amount of external precipitating stress Predisposition as determined by the basic personality makeup, intelligence, performance and history of past psychiatric disorders Impairment of functional capacity Psychological tests	American Transit Association Motorability Test

the psychological tests. This group had a *total accident frequency of* .497 A/M/M.

In Group 3, 51 candidates passed the motorability tests and did not take the psychological tests. This group had an accident rate of .412 A/M/M.

Group 4 consisted of 31 candidates who passed the psychological tests and did not take the motorability tests. The accident frequency in this group was .349 A/M/M.

In Group 5 there were 69 candidates, who passed both the motorability and the psychological tests. The accident frequency in this group was .308 A/M/M, the lowest in the study.

The results indicated that those operators selected under the new method, which includes psychological tests, had a lower accident frequency than those selected under the old method. Those who passed the motorability tests had a better accident rate than those who did not take the tests. *Psychological testing seems to be a finer discriminant than the motorability tests, and both are better than either alone.*

The statistical evaluation of the results of categories 3 and 5, using standard statistical methods,[11] established a critical ratio of 2. This indicated that only in 1 case in 20 could this difference in group accident rate have occurred by chance. Therefore, comparing these 2 groups (3 and 5), in 95 cases out of 100 the new selection method (Group 5) selects a group of operators who have a lower accident rate than a group selected by the old method (Group 3).

It is our opinion that the future development of a motor-vehicle accident-prevention program will depend on a better understanding of the psychological problems involved.

RESULTS

The comprehensive medical program we established resulted in:

1. A reduction of accidents of over 50 per cent
2. A decrease in absenteeism as a result of improved employee health
3. Substantial financial savings by the company

Operator selective control definitely reduced the frequency of accidents. In 1946 there was a total of 6,377 accidents. This number was reduced to 3,608 in 1950; to 2,568 in 1953; and to 3,130 in 1955. We believe that this reduction in accidents resulted from the detailed medical program, the profile classification and the introduction of psychological testing.

Improved Employee Health

It was shown that there was a decrease in illness following the development of a comprehensive medical program.[7] In addition, there was a substantial reduction in the number of industrial accidents. Payments made to employees for sick wages and association benefits for time off due to illness have been reduced since 1947. This is further evidence of reduced absenteeism and improved employee health.

Economic Results

The economic results are of particular importance to industry because of the substantial saving in money. There was a reduction in medical costs to our company after the Medical Department was reorganized in 1947. In 1946 the total medical cost was $256,424.71. Since 1947 the cost has been greatly reduced and in 1954 was $149,161.93. In 1955 it increased to $172,976.92. The over-all substantial reduction was effected in spite of the increased medical fees, compensation costs and sick benefits. These savings were accomplished by decreased absenteeism as a result of employee health, reduction in compensation costs and the reduction in accidents.

From our figures it is obvious that the cost of maintaining a medical department is less than the cost of one severe accident.

We feel that only a mentally and a physically healthy individual should be allowed to drive a motor vehicle, since medical fitness is the keynote of accident prevention.

RECOMMENDATIONS

Basic medical research must be completed to establish facts concerning the relationship between driver health (physical, psychological and mental) and accident prevention.

The effects of the following drugs on drivers must be studied: antihistamines, antihypertensives, tranquilizers, sedatives, stimulants and alcohol.

In industry, medical safety centers sponsored by industry and/or insurance companies should be responsible for preplacement and periodic examinations and training.

Education is a vital part of this program. Newspapers, magazines, television and radio must be utilized to educate the general public and the physician in their role in motor-vehicle accident prevention.

Private and commercial drivers must be educated by experienced safety engineers.

High-school students should be required to take a well-planned course in driver training as part of their curriculum, and the older driver should be expected to take prescribed training courses before obtaining his first license.

The solution of this complex problem requires the combined efforts of many groups: highway engineers must continue to improve the roads; the automotive industry must design cars for safety; the physician and licensing bureaus must permit only the qualified to drive.

REFERENCES

1. Accident Facts, 1955 edition, p 55, Chicago, Ill., National Safety Council.
2. Brandaleone, H., *et al.*: Recommendations for medical standards for motor vehicle drivers, J. Indust. Med. & Surg. 26:1, 25-32, 1957.
3. Brandaleone, H., and Daily, R. H.: A method of reducing the accident rate in bus operation-selection of the bus operator, Indust. Med. & Surg. 19:231, 1950.
4. Brandaleone, H., and Flamm, E.: Psychological testing—effect on the accident frequency of bus operators, Indust. Med. & Surg. 24:296-298, 1955.
5. Brandaleone, H., and Friedman, G. J.: An aid to accident prevention—medical profile classification of bus operators, Indust. Med. & Surg. 22:520, 1953.
6. ———: Medical aspects of accident prevention, Mass Transportation 48:11, 1952.
7. ———: Medical care in a surface transportation company, Indust. Med. & Surg. 21:174, 1952.
8. ———: Physical standards for vehicle operators—an aid to accident prevention, Indust. Med. & Surg. 25:17-22, 1956.
9. Cleeton, G. V., Kraft, M., and Royster, A.: A Manual of Instruction; American Transit Association Motorability Tests, rev., New York, A.T.A., 1947.
10. ———: A Manual of Instruction; Standard Examination for Transit Employees, New York, A.T.A., 1946.
11. Garrett, H. E.: Statistics in Psychology Education, New York, Longmans, 1953.
12. Maslow, A. H.: Security and Insecurity Tests, Stanford University, Cal.
13. Symposium: Medical aspects of motor vehicle accident prevention, New York, New York University-Bellevue Hospital Center, New York J. Med. 56:3853-3882, 1956.
14. Thurstone Temperament Schedule, Science Research Association, 57 W. Grand Ave., Chicago, Ill.
15. Waits, J. V.: The use of the American Transit Motor Ability Test in the selection of bus and street car operators, Proc. 26 Ann. Meet. Highway Res Board, December, 1946.

7

The Role of the Coroner in Motor-Vehicle Deaths

S. R. GERBER, M.D., LL.B.*

This mounting problem of motor-vehicle deaths has confounded everyone to the extent that all too many people have developed a fatalistic philosophy and have shirked all responsibility in the search for the true etiology and effective remedies. They hide behind such alibis as "the enormity of the problem," "the multiplicity and the diversity of the factors involved" and "the ever-recurring element of the instability of human nature." Many who have attacked the problem have studied it from the approach of individual and specific interests. While such individual approaches are necessary, there must be correlation of information and some degree of unification in the final analyses.

Basically, most of the factors involved have legal and/or medical implications. Logically, then, it should be the duty of the medicolegal authority, the coroner, to take the lead in his jurisdiction in stimulating co-operative effort to ascertain the basic causes for motor-vehicle accidents which cause deaths.

In many jurisdictions of the United States, the coroner is charged with the legal duty of determining the *mode and the manner of death, as well as the anatomic cause.* The determination of the anatomic cause of death requires the recognition and the evaluation of evidence presented by the dead body and a clinical history of the decedent. This is the medical phase of the coroner's responsibility. The mode and the manner of death are deduced from analysis of reports of investigation into the attendant circumstances correlated with results of studies of scientific evidence and facts developed from thorough examination of the body. When all factors are taken into consideration, the final verdict as to the cause, the mode and the manner of death is incorporated into an official document which may be used for legal purposes. It is apparent that the medical and the legal aspects of the coroner's duties are integrated to such an extent that one cannot be given pre-eminence or be disassociated from the other.

Coroners' investigations must be strictly unbiased and free of preconceived opinions. Rumors and clues must be sifted for facts.

---

* Coroner of Cuyahoga County, Cleveland, Ohio.

(In an era when the gross autopsy examination had fallen to ever lower levels of misunderstanding and indifference, Dr. Gerber's approach and reaction to his job and to his broader responsibilities in connection with it are most illuminating and refreshing. The fact that the autopsy investigation—and all it implies—is gradually regaining its former rank may be attributed largely to the keen interests of this kindly and self-driving personality toward *Truth* in all its varied forms. Dr. Gerber's analysis of the motor vehicle accident problem is a revealing one, which will be read with increasing interest and admiration. It is most regrettable that his article could not be presented here in its entirety; limitations of space prohibited this. At any rate, the [illegible] problem at the community level more than a knowledge of what this single doctor has done in this and related fields [Ed.])

All available facts must be sought out, recorded accurately in detail and considered carefully. Every conclusion must be the result of only a logical study of the facts. No statement should be made that cannot be substantiated by the facts. The final decision must be free of all influence of prejudices, hunches or assumptions.

In no field of the coroner's investigations is this more important than in establishing whether or not death was caused by accident. Murders and suicides may present the appearance of accident. Only a thoroughly objective investigation will disclose the actual situation. The failure to recognize murder is quite obvious. Where it is known that murders will be detected and the perpetrators punished, the community enjoys a greater sense of security than where there is presentiment that the cleverly conceived and concealed murder will not be detected. In ascertaining that death was caused by accidental means, rather than by murder, the coroner dispels the clouds of suspicion and unwarranted ignominy and disapprobation.

Attention must be directed to determining whether or not death during, following or even prior to an incident involving a motor vehicle was due to injury or natural disease. It must be taken into consideration that while driving or riding in a motor vehicle persons may be stricken with fatal "heart attacks," spontaneous cerebral hemorrhages or other sequelae of natural disease or previously inflicted violence. The vehicle with a moribund person at the wheel or as a passenger may become involved in a collision Persons run over while lying in the roadway or falling into the path of a moving vehicle must be examined thoroughly to determine whether or not death might have occurred prior to the time of the apparent accident.

A thorough autopsy must be performed in every case of death following involvement in a motor-vehicle accident. It is a neglect of duty on the part of the coroner to attribute a death to a motor-vehicle accident when it is actually due to pre-existing natural disease, suicidal poisoning or violence of homicidal origin.

The coroner must bear in mind that he has a responsibility to the welfare of all people, not only to those in his immediate jurisdiction but also to the country as a whole. The shortsighted coroner or physician would believe that the need for complete accuracy in determining the cause of death in these cases is purely academic. The many ramifications of erroneous certifications of causes of death are too numerous to mention here. However, one aspect should receive attention; that is where sympathy for the surviving relatives obstructs the long-range view of ultimate justice. With the thought that these persons ought to benefit from any possible financial settlement, death is attributed to the motor-vehicle accident involved. Where such remuneration is not warranted, it is an injustice to the company or the individual who is required to pay. The coroner should be aware of the fact that his decisions not only will affect the parties immediately concerned but, where an insurance company is involved, for example, they will have a bearing on the national economy. Every individual should realize that the purse of every insuree is affected by the number of payments made by insurance companies. When the number of deaths attributed to motor-vehicle accidents increases, the cost of protection for each insuree increases accordingly

Motor-vehicle deaths are classified statistically as "accidental," that is, due to accident as contrasted with deaths due to homicide, suicide, natural disease, etc. An erroneous concept of etiology leads to an outmoded fatalistic attitude toward accidents. An analysis of the true meaning of the term *accident* would seem in order. The Cyclopedic Law Dictionary defines an accident as

> an event which, under the circumstances, is unusual and unexpected by the person to whom it happens.
>
> The happening of an event without the concurrence of the will of the person by whose

agency it was caused; or the happening of an event without any human agency. . . . In Equity Practice: Such an unforeseen event, misfortune, loss, act or omission as is not the result of any negligence or misconduct in the party.

It must be inferred that few deaths in which motor vehicles are involved are caused by accident literally and in the full connotation of the definition. It is true that the event is unexpected by the victim but, in the circumstances, is it unusual? The happening of the event may be without the concurrence of the will of the person by whose agency it was caused, but in most instances the ultimate causation can be attributed to human failure, negligence or misconduct. That this interpretation is commonly accepted is demonstrated by the number of civil and criminal court actions against persons who were, or were thought to be, responsible for fatal or nonfatal injuries or property damage produced by motor vehicles. In the interest of civil as well as criminal justice, the coroner in his investigation to determine the responsibility of a motor-vehicle accident in causing death must be equally as thorough and objective as in the investigation to determine whether or not death was due to murder, suicide or natural disease.

In this age of science, few people believe that anything "just happens." The public, generally cognizant of the inexorable laws of cause and effect, rightfully expects that individuals who have the responsibility of making decisions will do everything in their power to search out all factors contributing to ultimate causation. People of this era refuse to accept complacently lethargic or fatalistic attitudes toward these "accidental" deaths

Since accidents do not "just happen" but are caused by factors which must be sought out, those directly responsible for public welfare must give attention to the remote, proximate and final causes of accidents. In discharging his duties the coroner must consider all aspects, not only of each case but of the summation of similar cases as well.

The coroner has a moral as well as a legal responsibility to conduct a thorough scientific investigation into all factors involved in causing the death of those persons who come under his jurisdiction. Furthermore, it is his duty to ensure that the specific information which he obtains is compiled in such a manner that it can be utilized to the best advantage in studies of related problems.

Information gathered and correlated in the coroner's investigation may be divided into two categories: (1) medical information—(a) anamnestic and (b) direct examination of the victim; (2) information ascertained in investigation of the accident and the attendant circumstances. To have any value in general studies, this information must be reduced to concise terminology which will facilitate statistical classification. Every coroner and coroner's physician must study the regulations of the Bureau of Vital Statistics and be familiar with the International Statistical Classification of Diseases, Injuries and Causes of Death.* Every coroner must understand thoroughly the Uniform Definitions of Motor Vehicle Accidents.† Only those rulings conforming to these definitions and classifications can be used correctly by other agencies interested in studies of traffic accidents.

There has been a growing interest in studies that attempt to correlate injuries incurred in automobile and aviation accidents with their causation. The coroner should be cognizant of the point of interest of these study groups and accordingly record information which can be integrated in such research. Actually, the coroner should be able to direct attention to further study of factors which in his experience he finds commonly recurrent in statistics compiled from ex-

* Bulletin of the World Health Organization.
† United States Government Printing Office.

amination of victims correlated with other ancillary information.‡

The exact anatomic cause of death cannot be established without a thorough necropsy performed by one experienced in pathology of trauma as well as pathology of natural disease. The clinical history is just as essential in evaluating the effect of injuries as it is necessary in guiding the attending physician in evaluating the effectiveness of therapeutic procedures. The reports of the accident investigation are required in establishing the mode and the manner of the death. The coroner should be able to assist the police by analyzing some pertinent information contained in the police reports in the light of the evidence ascertained in examination of the victim.

Presented in outline form, the numerous factors may give the impression that the suggested procedure for examination and investigation of vehicular fatalities is too detailed and involved to be practicable. No one would deny that every investigation of a murder must be thorough and every effort made to find the actual killer. There were more than 38,000 vehicular fatalities in the United States in 1955 as contrasted with a yearly average of approximately 5,000 homicides. All physicians, as well as coroners, have an obligation to strive to reduce the number of deaths from violence whether they result from "accidents" or deliberate homicides. The familiar role of etiology in directing effective preventive medicine must be applied to preventing deaths from motor-vehicle accidents. The true factors of causation must be revealed.

Here are some suggestions intended to direct attention to specific points of interest in any investigation of a motor-vehicle accident. For example, methods of first aid and treatment of the injured need to be evaluated in the light of unbiased facts. A practical study of this problem could be conducted through co-operation of the police, ambulance attendants, physicians and the coroner.

Most of the information indicated under accident investigation and ancillary information is included in report forms customarily used by the police, sheriffs and highway patrols. Where such forms are not used, the coroner should influence law-enforcement officials to adopt routine reporting on forms prescribed in their state. Factors recurring frequently will direct attention to the need for enforcement of laws and necessary changes in legislation, engineering and educational approaches.

No coroner should feel that his sole responsibility lies merely in determining accurately the cause of death in individual cases. Properly compiled, much of the information which is required in individual cases could serve the broader interest of attacking the problem of reducing deaths from motor-vehicle accidents. In order to be utilized for this purpose, it is necessary to correlate essential information for individual cases, and, since no comprehensive conclusions can be based on a "series of one case," statistical data must be compiled on the total number of cases.

A program for accident prevention must include studies of legislation, law enforcement, safety engineering and education. Each facet of the program reflects a different viewpoint. In order that the coroner may furnish suitable statistics most efficiently to each field of interest, he should consult with those responsible for each avenue of attack, ascertain what type of information each requires and devise suitable forms for compiling statistical data. He should work closely with the police departments, personnel of various news-reporting media and the local Safety Councils, and be able to supply statistical information which may show trends in accident fatalities. He should be

‡ The author has developed a most comprehensive Outline (15 pages) of Information Required in Coroner's Investigation of Deaths Due to Motor-Vehicle Accidents. Unfortunately, limits of space do not permit its inclusion here. [Ed.]

able to state the cold facts in answer to such questions as: Are the driver fatalities on the increase in the current year as compared with last year at this same date? What age group is represented most frequently in the driver or the pedestrian fatalities? What injuries are observed most frequently in the pedestrian fatalities?; in the driver fatalities?; in the passenger fatalities? How many driver and pedestrian fatalities were under the influence of alcohol at the time of the accident?

Pertinent information obtained from reports of accident investigation entered on the same page with the medical facts facilitates correlation of such data with the injuries.

The examination of clothing is a detail that frequently is neglected. In the interests of safety education and automotive engineering, it would be important to ascertain whether or not protection against impact injury was provided by clothing, accessories or articles carried in clothing. It might be assumed, for example, that heavy overcoats would offer such protection. On the other hand, accessories or articles carried in clothing might contribute or actually cause serious injuries, such as sharp objects which might be driven into the chest wall.

At the Cuyahoga County Coroner's Office a separate record for statistical purposes is made for each case. Pertinent information is copied from the coroner's records and the police reports onto keysort cards. It has been found that this procedure provides a reliable method of quick reference to furnish information on many specific questions as well as to facilitate compilation of accurate statistics.

Although the National Safety Council has been compiling detailed statistics on motor-vehicle accidents in the United States since the late 1920's, a study of their annual publication demonstrates that even though there has been a steady increase in the number of jurisdictions reporting, there is still a great need for more consistent uniform reporting. Coroners should co-operate fully with their local Safety Councils and be able to supply them with statistics in the forms that they require. The need for more thorough investigation into the contributory factors involved in motor vehicle accident causation and reliable reporting of statistics is seen when one studies the reports on alcohol incidence in vehicular accidents.

At the very beginning of the studies into the problem of vehicular accidents it was recognized that the driver and the pedestrian under the influence of alcoholic beverages constituted a factor that warranted attention. In spite of the fact that tests for alcohol are reliable, comparatively simple to perform and accepted as court evidence, too few jurisdictions have taken full advantage of this scientific aid to establish evidence that is important not only to the individual case but also to the problem as a whole. In some jurisdictions such tests are employed only in the case of the obviously intoxicated driver. In other places, only the questionable cases are tested. Some police test only the drivers involved in fatal accidents. The 1956 edition of *Accident Facts*, published by the National Safety Council, reflects how inadequate are the statistics on this problem. On page 53 of that publication, the following statements are made:

> In 26 out of 100 fatal accidents, a driver or an adult pedestrian had been drinking, according to reports from 20 states.

According to reports of the National Safety Council's Committee on Tests for Intoxication, chemical tests to determine the degree of intoxication in suspected drinking drivers were used in 45 states during 1953,* and as of July, 1955, 21 states had chemical test laws.† It is apparent that many jurisdictions using the tests are not supplying the National Safety Council with the information which they need.

The report from *Accident Facts* continues:

> Among the drivers involved in fatal accidents for whom condition was stated, 22 out of 100

* 1953 Uses of Chemical Tests for Intoxication
† Test Talk, July, 1955.

had been drinking. . . . The driver's condition was not stated in 27 per cent of the cases. . . .
Among the reporting states, drinking drivers ranged from 7 out of 100 drivers involved in fatal accidents to 45 out of 100. . . .
Among adult pedestrians involved in fatal accidents, 25 out of 100 had been drinking, . . . according to reports from 20 states. . . . The condition was not stated for 33 per cent of the pedestrians killed.

The fact that these statistics do not portray the true situation is implied by a study conducted in the State of Delaware on drivers in fatal accidents which is reported on the same page of *Accident Facts:*

Blood tests were made whenever possible of persons injured in traffic accidents, and blood samples taken or intoximeter tests given to drivers involved unless they refused. In all cases where injuries were too severe to permit tests, or the driver refused to take them, the investigating officer recorded his opinion on whether the person had been drinking.

Results of the study of drivers involved in fatal accidents in 1955 were as follows:
138 drivers were involved in 97 fatal accidents.
20 drivers (14.5% of the total) had .15 per cent of alcohol in their blood—considered to be definite evidence of "under the influence"
13 drivers (9.4%) had .05 to .14 per cent of alcohol in their blood—considered to be evidence of some degree of impairment.
3 drivers (2.2%) had less than .05 per cent of alcohol in their blood.
20 drivers (14.5%) who were not tested, had been drinking, in the opinion of the investigating officer.
The results of the study thus show a total of 56 drivers (40.6% of all drivers involved in fatal accidents) as "had been drinking," either by test results or by observations of the officer investigating the accident.

These findings approximate the results of studies made in the author's office over a period of 19 years (1937-1955) (Table 5). Blood for alcohol determinations are drawn from all fatalities received at this office who are over 15 years of age and have survived less than 12 hours following the accident. By this regimen about 55 per cent of the victims of vehicular accidents were tested in the 19-year period. In the tested cases, alcohol was found to be present in 46 per cent of the pedestrians, 54 per cent of the drivers and 42 per cent of the passengers. These statistics present only one aspect of the situation, that is, as they relate to the deceased victims. Some of the victims tested had survived a sufficient length of time to metabolize alcohol present at the time of the accident and, therefore, contributed to the number of negative tests. Taking into account also the fact that we have no figures on the number of drinking drivers who may have caused the death of alcohol-free victims, *it seems apparent that these statistics are most conservative.*

The question arises as to the ratio of nonaccident drivers to accident drivers. Such a survey was conducted in Toronto, Canada, during the period from December, 1951, to November, 1952.* It was found that only 8.7 per cent of the nonaccident drivers tested had an alcohol content of 0.05 per cent or more, contrasted with 22.5 per cent of the drivers involved in accidents who were tested.

There is need for a study to be conducted as a co-operative effort of the coroner, the law-enforcement officials and the treating physicians to determine accurately the true incidence of alcohol in fatal and nonfatal motor vehicle accidents. *It seems strange to the author that blood-alcohol determinations are not routine clinical tests in all accident cases received at hospitals.* Certainly, the blood-alcohol values can be of great assistance in assessing the etiology of coma, irrational states and other manifestations that might be attributed to injury when actually due to alcoholic intoxication or vice versa. A question that arises and warrants further study is whether or not alcohol concentration in the body at the time of injury affects the clinical course in brain-injury cases. Routine blood-alcohol determinations on ad-

* Lucas, Kalow, McColl, Griffith, Smith: Proceedings of the Second International Conference on Alcohol and Road Traffic, p. 142.

mission to the hospital would contribute valuable information for such a study.

To summarize, the role of the coroner in motor-vehicle deaths is:

1. To determine accurately the anatomic cause of death in *every* case by complete and thorough autopsy examination of the body and study of the clinical history.

2. To require a detailed report of the investigation of the accident and *all* factors involved.

3. To study and evaluate critically all medical and investigative information.

4. To base all official rulings on facts alone.

5. To record all facts in a manner that can be utilized efficiently (Table 6) (a) to substantiate the official ruling and (b) to supply statistical data that can be utilized by departments and organizations engaged in national surveys of this problem.

6. To instigate and participate actively in studies to determine the true etiology of these unnecessary deaths.

If the coroner's investigations are to serve a broader purpose than the mere solution of the immediate individual case, it is apparent that he must have the active assistance of many people who have specialized knowledge and experience in the diversified fields of interest involved directly or indirectly. Some of these include law-enforcement officials experienced in accident investigation, physicians treating the victims, pathologists trained in medicolegal examinations, statisticians and safety educators.

Some physicians who read this treatise may consider that this is a wholly idealistic approach practicable only in a large metropolitan area. Many of the physicians and surgeons who read this text may practice in jurisdictions where the coroner is not a physician; therefore, they may regard such an approach impossible in their communities. It cannot be stressed too strongly that this program calls for complete co-operation, mutual understanding and interest.

As stated previously, the coroner's office is both medical and legal in its duties and responsibilities. Neither the medical nor the legal aspects can be neglected; nor can one be given pre-eminence. To function at its best, the office requires the co-operation of representatives of both the medical and the legal professions in the community. It is recognized that in many states there is need for modernization of laws governing medicolegal investigations of deaths in which violence is suspected to be involved. *The nationwide increase in deaths due to motor-vehicle accidents should arouse every community to action.* Practicing physicians should acquaint themselves with the legal implications which the coroner must consider. Attorneys should become familiar with the problem of evaluating the medical aspects involved. The coroner, if he is neither a physician nor an attorney, should consult experienced members of both professions. Individual members of the legal and the medical professions will find that through such co-operation they will gain valuable practical information. The community as a whole will be benefited.

Through the media of the press, radio and television, the public is being warned of the ghastly spectre that stalks our highways, causing more civilian casualties in one year than our military casualties of 3 years' action in Korea. The estimated monetary loss resulting from motor-vehicle accidents in one year ($4,500,000,000 in 1955) is so enormous that the average person does not grasp the significance. Such statistics have little effect on the irresponsible driver. Fatal motor-vehicle accidents that occur in or near smaller communities are much more realistic to the residents, many of whom may have some personal relationship or contact with the victims. (The National Safety Council reports that in fatal accidents 62 per cent of the drivers lived within 25 miles of the accident and 20 per cent lived elsewhere in the state.)

The total number of accidents in one of the smaller communities may seem relatively small when compared with the toll in a large

city. However, three fourths of the motor-vehicle deaths in the United States in 1955 resulted from accidents in rural areas. Obviously there are more rural areas. This illustrates the relative significance of isolated and compiled statistics. Also, it emphasizes the need for accurate data on motor-vehicle accidents in rural areas.

Every citizen must be made to realize the significance of accidents in his own community. Safety education through informing the public of what, where and how accidents occurred in the local community is more effective than staggering statistics of a national scope. Of course, such statistics can be compiled only from accurate reporting from each community. Every driver must be brought to the realization that the privilege of operating a motor vehicle carries a tremendous responsibility for the safety of others. Every manufacturer of motor vehicles must accept his responsibility to strive for safety, not only in engineering but also in the psychological effect of advertising. Those officially concerned with the welfare and the safety of the community must direct their attention not only to penalties for infractions of existing laws but also to instituting preventive measures.

The Committee on Public Information reported to the President's Highway Safety Conference in 1949:

> The responsibility is clear in the case of public officials to make readily available to the public all pertinent facts concerning their highway safety activities.

A coroner should not be expected to expend the time, effort and public funds to compile this information unless he has some assurance that it will be used to the advantage of the community. Therefore, it behooves those interested in specific phases of these problems to demonstrate this interest to the coroner and work with him in obtaining, compiling and correlating such information. This can be effective only if it is a long-range program with sustained interest. It must be a community project with physicians, attorneys, law-enforcement of-

TABLE 5. VEHICULAR FATALITIES—YEARLY COMPARISON AND ALCOHOL INCIDENCE —CUYAHOGA COUNTY 1937-1955

Year	Number of Cases			% Decrease from 1937	Incidence of Alcohol		
	Males	Females	Total		Males	Females	Total
1937	274	76	350		60.7%	30.6%	54.7%
1938	178	56	234	33.1%	57.3%	40.4%	53.5%
1939	175	49	224	36.0%	57.4%	40.0%	54.5%
1940	152	39	191	45.5%	55.7%	33.3%	53.6%
1941	187	68	255	27.1%	63.6%	19.4%	51.8%
1942	183	42	225	35.6%	65.6%	43.7%	62.5%
1943	134	45	179	48.7%	45.0%	25.0%	41.0%
1944	132	45	177	49.3%	47.0%	35.0%	44.0%
1945	138	29	167	52.2%	55.0%	35.0%	52.0%
1946	174	39	213	39.1%	55.0%	35.0%	52.0%
1947	153	48	201	42.6%	51.0%	32.0%	45.0%
1948	132	34	166	52.6%	48.0%	0.0%	40.0%
1949	117	46	163	53.4%	52.0%	25.0%	44.0%
1950	118	41	159	54.3%	52.0%	30.0%	48.0%
1951	144	27	171	51.1%	45.0%	19.0%	40.5%
1952	156	49	205	41.1%	43.0%	19.0%	37.0%
1953	183	41	224	36.0%	42.0%	9.0%	37.0%
1954	129	48	177	49.4%	50.0%	19.0%	42.0%
1955	135	38	173	50.6%	51.2%	17.4%	44.0%

Table 6. Vehicular Fatalities 1954— Major Injury and Survival Interval

Major Injury	Pedestrian: Total	Pedestrian: DOA*	Pedestrian: Less Than 12 Hr.	Pedestrian: 12–24 Hr.	Pedestrian: 1–8 Days	Pedestrian: More Than 7 Days	Driver: Total	Driver: DOA	Driver: Less Than 12 Hr.	Driver: 12–24 Hr.	Driver: 1–8 Days	Driver: More Than 7 Days	Passenger: Total	Passenger: DOA	Passenger: Less Than 12 Hr.	Passenger: 12–24 Hr.	Passenger: 1–8 Days	Passenger: More Than 7 Days	Total: Total	Total: DOA	Total: Less Than 12 Hr.	Total: 12–24 Hr.	Total: 1–8 Days	Total: More Than 7 Days
To brain.																								
With fracture of skull only	11	2	3	2	2	2	6	3	3				10	4	3	1	1	1	27	9	9	3	3	3
With fracture of skull and body fractures	24	9	8	1	5	1	12	6	3	1	2		7	4	3				43	19	14	2	7	1
Without fracture of skull	2	1			1		4				3	1	2	1		1			8	2		1	4	1
Without fracture of skull but body fractures	5	1	3			1	2			1	1		3		1	1	1		10	1	4	2	2	1
Total	42	13	14	3	8	4	24	9	6	2	6	1	22	9	7	3	2	1	88	31	27	8	16	6
To spinal cord.																								
With fracture of vertebra	4	4																						
Without fracture of vertebra													4	3			1			8	7		1	
Total	4	4											4	3			1			8	7		1	
To chest:																								
With fracture of thoracic cage	10	6	2		2		11	7	3		1		9	5		3	1		30	18	5	3	4	
Without fracture of thoracic cage	1				1		1					1							2				1	1
Total	11	6	2		3		12	7	3		1	1	9	5		3	1		32	18	5	3	5	1
To abdomen																								
With fracture of pelvis	10	2	4	1	1	2													11	2	4	1	1	3
Without fracture of pelvis	7	2	2		2	1	1	1					1					1	8	3	2		2	1
Total	17	4	6	1	3	3	1	1					1					1	19	5	6	1	3	4
To extremities	2				1	1													2				1	1
Multiple injuries	15	3	9	1	2		6	3	1			2	2	2					23	8	10	1	2	2
Miscellaneous	1					1	1	1					2	2					4	3				1
Grand total	92	30	31	5	17	9	44	21	10	2	7	4	40	21	7	6	4	2	176	72	48	13	28	15

Note: "Major injury" signifies most severe injury *to which death is attributed and is not to be construed as the only injuries*. In "multiple injury" classification the majority of cases received such severe injury to chest and abdomen that *no one* injury could be selected as the cause of death.

*DOA—Dead on arrival at hospital

ficers, insurance investigators, statisticians, automobile sales and service managers, fleet operators and news reporters meeting with public officials at regular intervals to outline and correlate methods of approach, discuss progress and compare what is being done in other communities throughout the nation. Since it is the coroner who has the need in his routine investigations to study many of the factors involved in fatal motor-vehicle accidents, he should spearhead the organization of such a community project.

ADDENDUM

The following excerpts are from the author's statistical reports as Cuyahoga County Coroner, which illustrate compilation of data on vehicular fatalities by him in this chapter:

We who have been associated with studies of vehicular accidents and methods for reducing highway slaughter derive a sense of accomplishment and justification for our efforts when we look at the record and compare the 1937 total of 350 vehicular fatalities in this county with 173 in 1955. This reduction is even more impressive when related to the increase in the number of gallons of gasoline consumed and the number of miles traveled. Although it is discouraging to see the same factors of causation and incidence repeated year after year, the cure must be found; remedies will not suffice.

In 1946, in our 10-year survey of vehicular fatalities, we wrote as follows:

"From the factors most commonly recurring, the average vehicular fatality is represented by the following delineation: a male pedestrian over 50 years of age, a skilled laborer, who drops in at the neighborhood tavern for his social drinking on a Saturday, or perhaps on Sunday attends a party at which liquor flows freely. From these averages we can state, furthermore, that such an individual is more likely to be killed in the month of October between the hours of 6·00 P.M. and midnight in clear weather when the pavement is dry and the street lights of average type."

Eight years later, what do we find? In 1954, the highest monthly incidence occurred in January and October. All other factors remained essentially the same. Thirty-seven per cent of the victims were male pedestrians; 40 per cent of the male victims were over 50 years of age, 53 per cent were skilled laborers. In 1954, accidents occurring on Saturday accounted for 23 per cent of the fatalities from vehicular accidents; on the basis of the 12-year average the proportion was 19.8 per cent. The alcohol incidence for Saturday was 41.9 per cent of the tested cases in 1954 and 44.6 per cent in the 1943 through 1954 period.

Thirteen per cent of the fatalities in 1954 resulted from accidents which occurred on Sunday with 53 per cent of the tested cases showing presence of alcohol. For the 12-year period the comparative figures were: 16 per cent from accidents occurring on Sunday and 55 per cent of the tested cases had alcohol present in their blood. In 1954, accidents occurring on Friday, Saturday and Sunday (about 43% of the week) caused the death of 55.6 per cent of the vehicular fatalities; 39.3 per cent of the tested cases for these days had positive tests for alcohol. The figures for the 12-year average showed that 51 per cent of the fatalities resulted from accidents which occurred on Friday, Saturday and Sunday, and 48.6 per cent of the tested cases showed the presence of alcohol.

Fifty-eight per cent of all vehicular fatalities resulted from accidents occurring between the hours of 6:00 P.M. and midnight in 1954, and 45.5 per cent of the cases tested had alcohol present. In the 12-year period, 36 per cent of all vehicular fatalities resulted from accidents which occurred between 6.00 P.M. and midnight and nearly one half of these (47%) resulted from accidents which occurred between 6:00 P M. and 9:00 P.M. When the 24 hours are divided into 8-hour periods beginning at 7:00 A.M., it is found that 47 per cent of the fatal accidents occurred in the 3:00 P.M. to 11:00 P.M. period, and nearly one third (33.1%) occurred in the 11.00 P.M. to 7:00 A.M. period. More than three fifths of the fatal accidents in the latter period occurred in the 4-hour period of 11:00 P.M. to 3.00 A M.

Persons charged with the responsibility of fostering safety in transportation have been making detailed studies of "crash injuries." With this thought in mind we have compiled tables correlating the type of major injury with the survival period subsequent to the accident and the ages of the pedestrians, drivers and passengers. The major injury is considered as the most severe injury to which death is attributed and is not to be construed as the only injury sustained. In considering the total of the 2-year study (1953-1954) it is seen that nearly one half (48.5%) of the deaths were attributed to injuries to the brain. This was the leading cause

of death for pedestrians, drivers and passengers with 53.8 per cent of the fatalities due to brain injury. The survival period may be construed as indicative of the severity of the injury. It is seen that 71.7 per cent of the drivers whose death was attributed to brain injuries died immediately or within 12 hours, 41.5 per cent of these individuals were dead on arrival at the hospital. In the passengers it is noted that 67.3 per cent died immediately or within 12 hours, and 36.7 per cent were dead on arrival at the hospital.

Injuries to the chest caused the death of nearly one fourth (24.3%) of the drivers, with 85 per cent dying immediately or within 12 hours; 59.3 per cent of whom were dead on arrival at the hospital. The passengers closely approximated the drivers. The pedestrians presented a strikingly different picture, with 13 per cent of these fatalities attributed to chest injuries, 61.5 per cent dying immediately or within 12 hours, and 23 per cent of these being dead on arrival at the hospital.

Major injury to the abdomen and major injury to the chest were seen with equal frequency in pedestrians, but more of the persons with abdominal injuries survived more than 12 hours. About 3 per cent of the passengers and 3.6 per cent of the drivers died because of major injury to the abdomen. None of the passengers but about one half of the drivers died within 12 hours after receiving such injuries.

In about one seventh of the vehicular fatalities in the 2-year period, injuries to both the chest and the abdomen were so severe that the cause of death in these cases was attributed to "multiple injuries of chest and abdomen." The incidence of pedestrians and drivers in this category was nearly the same—16.7 per cent and 16.2 per cent, respectively. The proportion of persons dying immediately or within 12 hours was likewise similar—72.7 per cent of the pedestrians and 72.2 per cent of the drivers. However, a lower percentage of pedestrians sustaining such injuries were found to be dead on arrival at the hospital (21.2%) as compared with 38.9 per cent of the drivers. While only 7.7 per cent of the passengers sustained this type of injury, the severity is to be noted in that none survived more than 12 hours.

The correlation of the age group, survival period and major injuries to pedestrians, drivers and passengers is included in this report for those who are concerned with crash-injury studies We do not feel that in this 2-year study of 400 cases there is a sufficient number of cases in each age group on which to draw definite conclusions and interpretations. The age incidence in pedestrian, driver and passenger fatalities, however, is of general interest. It is seen that in the 2 years nearly 71 per cent of the pedestrian fatalities were over 50 years of age, while 78 per cent of the drivers and nearly 52 per cent of the passengers were between 20 and 50 years of age.

8

Prevention of Motoring Accidents from the Military Standpoint*

COLONEL JOHN R. HALL, JR., MC, USA
and
CAPTAIN HOWARD L. BLANFORD, MSC, AUS

Manpower losses due to injuries received in motor-vehicle accidents have become a major problem for military leaders and their staffs. The civilian heads of the Department of Defense and of the three military departments are fully cognizant of the problem and have directed studies of it and taken the corrective action deemed necessary. Military physicians play an important role in stimulating interest in and study of these manpower losses and their attendant suffering and death. Many staff and administrative agencies join in attempting to reduce these accidents.

(The editor's interest in motor-vehicle accidents began, from the standpoint of extraclinical factors, with his tour of duty in the naval medical corps in World War II, especially after his return to stateside hospital work. The naval emphasis on prevention was a novel, stimulating and sometimes perplexing point of view to this naive therapeutically minded orthropaedist. However, the inoculation took. The picture produced by the mangled bodies from motor-vehicle accidents soon displaced that of the combat zone and was—if that is possible—even more depressing. It is no wonder that the armed forces have been so instrumental in advancing all kinds of researches with regard to motor-vehicle accidents in particular. This is an activity of which the taxpayer has not been told enough. Perhaps the chapter by Colonel Hall and Captain Blanford will serve to orient our readers in this regard. At any rate, the editor is proud to present this brief report on the military aspects of motor-vehicle accidents. The reader, in turn, will be proud of the achievements in this connection by the armed forces medical people.)

Since this chapter is written from the Army viewpoint and by Army Medical Service personnel, it will emphasize that viewpoint. However, the United States Navy and Air Force have similar interests and well-developed programs.

Since the dawn of military history, leaders have been confronted with appreciable manpower losses due to nonbattle injuries and disease. Motor-vehicle trauma is merely another and newer category of nonbattle injury. The tremendous impact of the automobile and the truck upon civilization is reflected in the military establishments. United States Army figures, however, reveal that nonbattle injuries accounted for over 100 admissions to hospital per 1,000 average strength per year from 1819 through 1917 and from 1920 through 1942. During the first period mentioned, rates above 200 per 1,000 average strength were recorded, virtually uninterrupted, from 1821 until 1898, with the rate climbing above 300 from 1850 through 1860. By comparison, rates for the period 1947 through 1953 were consistently below 70 per 1,000 average strength, except for the years 1950 to 1951, when they were between 70 and 80. For the year 1953, for which data have been analyzed, evaluated and published, deaths from motor vehicles far exceeded those from instrumentalities of war, aviation accidents, occupational in-

* The authors acknowledge the valuable assistance given by the Army Safety Director and the Safety Directors of various Army agencies and commands in assembling the data for this chapter.

juries, poisonings or other causes, the rate being 62.3 per 100,000 average strength.[10] Of these, the ratio of off-duty to duty accidents was higher than 2 to 1. For 1953, 1.3 individuals per 1,000 strength were separated from the Army for physical disability incident to nonbattle injury.[11] Figures of other years reflect similar experience.

There is little question, then, that motor-vehicle trauma is an important cause of military noneffectiveness. Such manpower losses are of grave concern to military commanders and civilian leaders. The agent is new, but it is well known that uncontrolled nonbattle losses can be catastrophic. For example, in 218 B C., in war against Rome, Hannibal started over the Alps with 46,000 men. Fifteen days of the steep and treacherous trails are said to have cost him 20,000 accident victims and to have had a major effect upon his campaign. There can be little wonder that the commander has always been concerned with such losses.

For many years military physicians were among the more vigorous advocates of corrective programs to reduce avoidable manpower losses, especially needless injury and death caused by preventable accidents. That interest in losses due to accidents goes to the beginning of United States military history is borne out by von Steuben's first Army Regulations, in which he required physician attendance to their regiments on the march as well as in camp for the specific purpose of providing immediate proper care to accident victims.[12] There is further evidence in the writings of the military surgeon James Thacher. This physician described his experiences with accidental trauma in his Military Journal, covering the period 1775 to 1783 during the American Revolutionary War.[23]

During the 19th century and early in the 20th century, accidents were considered by many to be caused by events beyond control, they occurred despite preventive planning. Physicians were on the verge of the discovery of the causative organisms of disease and later, of the development of preventive medicine technics and procedures (Walter Reed and William Crawford Gorgas). However, the successes of these medical efforts gradually narrowed the gap between death rates for disease and nonbattle injury.[13] This focused the attention of military medicine upon the toll of accidents and stimulated preventive-medicine approaches to the problem. In the Annual Report of the Surgeon General, U. S. Army, 1932, note was made of the increase in relative importance of injuries as a cause of death, and the role of automobiles, as well as airplanes, in contributing to manpower loss was the subject of comment.[13] In the 1930's reporting systems were improved to provide better epidemiologic type information concerning accidental injuries. The 1940 Annual Report of the Surgeon General of the Army emphasized the importance of individual study of each case by commanders and medical officers in order to develop preventive measures.[14]

Military physicians, writing in *The Military Surgeon* in 1940[1] and 1942,[2] emphasized the roles of the medical officer and the commander in the study of accidents and the development of prevention programs. The role of the automobile and the truck again was emphasized.

As has been indicated, prior to mobilization for World War II, safety activities in the United States Army were carried out in varying degrees by organizational segments, the emphasis naturally being placed on those hazards peculiar to the individual segment. The first co-ordinated Army safety program as such was established in 1942 as part of the Plant Protection Program of the War Department. This later became the Internal Security Program.[16]

Of greatest concern in the first year of World War II was the prevention of losses from sabotage and subversive activities in industrial plants engaged in war production. It soon became evident, however, that the greatest production losses and delivery delays were due to accidents. The safety portion of the program developed to meet this situation paid great dividends among the

civilian support activities of the Army. In some measure it was carried into programs affecting military personnel. However, in 1944, the Director of the Occupational Health Division, Preventive Medicine Service, became concerned with the high military admission rate to Army hospitals because of nonbattle injuries. He recommended the establishment of a military accident prevention program under the auspices of the Surgeon General. The importance of accident prevention and the role of the Army Medical Service in co-operation with other agencies, which had already been in effect, was emphasized and expanded. By this time the policy and the procedures governing accident prevention in the Internal Security Program had been greatly expanded as the Services of Supply Safety Program, established on August 31, 1942.

In December, 1942, the War Department Safety Council had been organized, with medical representation.[16] During the war years, change in and expansion of programs were rapid. The safety portions of various programs that evolved during the period were so successful in the conservation of manpower that the Army Safety Program was formally established by regulations in 1946.

The current Army Safety Program is specified by Army Regulations 385-10 dated August 30, 1956. Safety is a responsibility of command, and staff supervision is exercised by a member of the Commander's staff, usually the Personnel Officer or G1, since such activities are concerned with the conservation of personnel.[18] *Medical activities dealing with safety are the responsibility of the staff medical officer, whose title is Surgeon.* Traffic and police matters are vested in the Provost Marshal.[20] Military Engineering, to include roads and other avenues of land communication, is the responsibility of the Engineer.[19] This includes recommendations for traffic regulations as indicated by the physical condition of roads and bridges, as well as the posting of signs for route marking and traffic control on permanent routes.

Safety aspects of transportation activities are of great concern to the Transportation Officer, who is the Commander's principal adviser on transportation.[22] Other staff officers have functions related to safety. Above all, the "Commander alone is responsible for all that his unit does or fails to do. He cannot delegate this responsibility."[17] While these assignments of responsibilities are purposely quoted from a manual which is issued as a guide for field operations, the same general subdivisions are found at all echelons of the Army, from Department of Army throughout subordinate commands and units large enough to have staffs.

At Department of Army level there is a full-time Army Safety Director assigned to the office of the Deputy Chief of Staff for Personnel. He is assisted by specialists in the various aspects of safety. Each major command of the Army and the chief of each technical service have a safety officer and such supporting personnel as are indicated. Safety officers are designated for each command of the Army down to unit level.

The motor vehicle as it relates to the Army and its personnel, both military and civilian, represents a major accident potential. The Army vehicle, with some one and one half billion miles of operation annually, is susceptible to accident involvement wherever operated. As a conventional vehicle driven over the highway, it becomes a part of the civilian traffic and the traffic accident problem. Convoy movements, although inherently well controlled, increase the accident potential on the highway due to increased traffic density. Tactical employment of Army motor vehicles off the highways has accident potential due to numbers and terrain. This problem is further aggravated by blackout driving, exercises and simulated warfare.

Army motor vehicles and those under contract to the Army transport a large portion of the nation's ammunition, explosives and other hazardous material. Many Army personnel, when off duty, drive cars of their own or are passengers in private vehicles or

are pedestrians. In each instance these individuals become part of the national traffic stream and a national motor vehicle accident potential.

Most civilian employees of Army installations travel to and from work in motor vehicles. The post complement who live on the post also drive automobiles. Many posts have troop populations that run well into five figures. The day-to-day business of a post, in terms of vehicular movement of personnel and supplies, is comparable with that of a city equal in size with its road system, congestion and complexity.

Driving conditions outside the United States require that additional instructions be furnished Army motor vehicle operators. Indigenous personnel in many areas have a marked disregard for safety precautions. *Speed limits do not exist in many countries.* Often there are narrow cobblestone roads and streets, which can be blocked by a single vehicle. Frequently buildings are found to be built flush with the roadside with doors opening outward. In many areas there are practically no shoulders on roadways and no sidewalks to handle the flow of foot traffic through towns and villages. A great many of the vehicles in operation are slow-moving contrivances, including many unlighted animal-drawn or human-propelled conveyances. *In some countries there are as many as 13 to 14 million bicycles in use.* This situation is further complicated during nighttime by poor street-lighting facilities and the custom of wearing dark clothing.

Experience continues to indicate that hospitalization for *motor-vehicle injuries* imposes a greater workload on Army medical treatment facilities than do injuries from other nonbattle causes. To illustrate: in 1954 the average duration of stay in Army medical treatment facilities for all nonbattle injury admissions was 22 days. During the same period noneffectiveness produced by motor vehicle accidents averaged 38 days per admission These figures include some bias, since they do not include patients separated from service and transferred to Veterans Administration facilities in patient status.

SELECTION AND LICENSING OF DRIVERS

Any person operating an Army motor vehicle must possess a valid U. S. Government operator's permit secured under the provisions of the standards established or maintained for other agencies by the Army. *These standards concern selection, testing* and *training of drivers.*

RECORDS AND PERMITS

A record is maintained of each individual qualifying for an Army driver's permit. All test scores, remedial training, retesting and other qualification data are kept on this record throughout the driver's employment or assignment. This record is analyzed periodically to determine expiration date of permit and need for remedial training. It is also reviewed immediately after an accident or upon reassignment to determine the need for re-examination, corrective measures or other specific remedial training.

Drivers' permits are renewable every 2 years unless otherwise prescribed. The renewal procedure consists of an examination of the driver's record card to ascertain his accident record and extent of traffic violation. *Renewal may be denied on the basis of accident record and traffic violation and upon the recommendation of the medical officer in case of physical limitations.*

Permits may be suspended and revoked for cause at any time.

DISPATCH AND MAINTENANCE

Before any Army vehicle is taken from a motor pool, the driver must possess a "Vehicle and Equipment Operational Record" authenticated by an authorized dispatcher. One portion of this form pertains to preventive maintenance services that must be performed by the driver before, during and after operation. In addition to these daily maintenance checks, the driver is also re-

quired to examine, at weekly intervals, drive belts, battery, antifreeze when being used and condition of the tires. Every driver is authorized to secure immediate off-post repair to his vehicle where continued operation could result in a breakdown or an accident.

ENGINEERING, ENFORCEMENT AND EDUCATION

The design, the construction and the maintenance of roadways on Army property over which the Department of the Army has jurisdiction must conform where practicable to standards in general use.[8,21] A definitive, considered enforcement program is functioning at all Army installations. Enforcement is on a selective basis directed at specific violations, since these have been shown to be primary accident causes. Standard penalty codes have been developed, and equitable adjudication of charges is required. Close co-operation is maintained with civil enforcement agencies.

In order to minimize the need for disciplinary action and at the same time provide an equitable basis for such action, precise and understandable rules and regulations have been drawn up and publicized on transportation of personnel; co-operation with civil authorities and civil traffic regulations; directives applicable to Army convoy operations; compliance by general transport vehicles, ambulances, fire trucks and other emergency vehicles with local and state speed limits and other applicable civil regulations; winter driving; transportation of explosives and other dangerous articles; towing of vehicles; operation of trailer-type vehicles; precautions against fire and asphyxiation; and highway warning kits.

INCENTIVES AND AWARDS

A program of safety awards and other incentives has been established to recognize both individual and groups of military and civilian drivers of Army motor vehicles for outstanding effectiveness in the prevention of motor-vehicle accidents and outstanding safe-driving performances. A large variety of awards, bestowed with proper publicity, are used.

OFF-DUTY MOTOR-VEHICLE ACCIDENTS

History continues to repeat itself in that off-duty motor-vehicle accidents, particularly in the United States, where greater opportunity exists for the use of private vehicles, contribute greatly to noneffectiveness. In 1952, during the conflict in Korea, off-duty accidents caused 632.8 admissions per 100,000 average strength in the United States, while the on-duty admissions rate was 579.5. Overseas, the on-duty admission rates per 100,000 average strength was 811.5 as compared with 111.8 for off-duty motor-vehicle accidents. Total Army rates for these categories were 686.2 on duty and 393 1 off duty. For every 10 deaths from combat there were 4 from motor-vehicle accidents. *For every soldier dying as the consequence of infective or parasitic disease in 1952, 10 died from motor-vehicle accidents.*[3] There is slight wonder that preventive medicine officers reflect and reinforce the concern of commanders, safety officers and other staff members concerning manpower losses from motor vehicles.

The off-duty motor-vehicle safety program starts on the post Billfold insert cards dealing with the responsibility of the individual while off post are given to all personnel on leave or pass, and safety slogans are stamped on liberty passes. Many installation commanders are making passes effective at noon or earlier in the day and terminating at noon or before nightfall, so as to preclude the necessity for driving after dark. Others set limitations on the distances to be traveled by privately owned vehicles. During holiday-leave periods, many commanders send letters to the families of military personnel asking their co-operation in helping to make the soldiers' off-post travel as safe as possible.

Motor-vehicle safety training is integrated into the orientation program of overseas returnees. The remedial driver training classes previously discussed are also widely utilized for military personnel apprehended for moving traffic violations or other citations by military or civilian police. Some large installations also utilize these remedial driver training classes for dependents of personnel stationed at the installation.

Installation commanders have initiated and are maintaining a continuing program of orientation and discipline to eliminate the practice of soliciting rides on public highways and thoroughfares by Army personnel signaling vehicles in any manner or by standing or walking on the traveled portion of the roadway in the direction of traffic. On the other hand, the establishment and the use of properly authorized and established "share-the-ride" or similar stations are encouraged.

Pre-embarkation training in driving customs of the country to which the individual is ordered is conducted. Other positive steps taken in overseas areas include closer liaison with foreign country traffic officials and organizations; active participation in periodic traffic safety campaigns conducted by countries in which United States troops are located; safety educational campaigns in foreign country schools and for the general public; continuing Army motor vehicle operator education; safety poster programs with the poster message printed in the particular foreign language; special accident prevention courses for indigenous driver personnel; talks on motor vehicle accident prevention as part of the troop Information and Education Program; meetings to discuss accidents and accident causes, participation by Army personnel in local civic group meetings; utilization of foreign country press and radio; augmentation of civil enforcement personnel by military police, and improved planning of Army motor vehicle traffic to meet foreign country road and traffic control limitations.

ARMED FORCES EPIDEMIOLOGICAL BOARD

The Armed Forces Epidemiological Board, the successor of the "Army Epidemiological Board," founded in January, 1941, is a joint agency of the Army, the Navy and the Air Force under the management and the control of the Secretary of the Army. The purpose of this board is to provide the military departments with scientific and research assistance and advice on matters pertaining to problems in Preventive Medicine. The board is made up of several commissions, one of which is the *Commission on Accidental Trauma.* This commission has taken cognizance of the morbidity and the mortality resulting from accidents caused by land vehicles and mechanical equipment in general. The individual projects of the commission have been developed to constitute a broad program and to utilize differing approaches to the problem of accidental injury. The mathematical and the analytical studies of accident causation have now reached the point where pilot applications have been made of technics for evaluating risk-taking in industrial and highway situations. An application of statistical quality control methods for the reduction of highway accidents has been demonstrated to be useful in accident prevention.

In the survey of personnel and interpersonnel factors in highway accidents, data have been collected through comprehensive psychiatric and psychological measures on subjects having varied accident experiences. Progress has been made in the development of adequate criteria of accident experience and in the statistical analysis of the relationships between the accident criteria and the psychological characteristics.

In the study of man's area of vision, emphasis has been placed on the development of better windshield-wiper patterns and installation. Marked improvements in the areas of visability result from the variable angle wiper design, using arrangements of

2 and 3 wipers. Further development of testing and measuring devices and technics for more reliable description of man's visual area has been accomplished.

Experiments have been completed which show that as people age they show a marked decrease in ability to see under low levels of illumination. Research currently is in progress on the combined effects of age and the limitations imposed on vision by the use of tinted windshields in an attempt to evaluate the practical importance of this problem for the older driver.

In the Crash Injury Research Project, data were gathered from seven states. The volume of case histories from these sources exceeds 1,500 cases per year based on the exposure of about 3,500 individuals to impact forces. One finding was that ejection from the automobile was the most common cause of injury in crashes. Ejection was found to double the risk of sustaining a moderate-to-fatal injury and that doors were forced open in about 50 to 75 per cent of cases involving injury accidents. One of the better-known results of these studies, sponsored initially by the Armed Services, is the adoption of safety devices indicated on the basis of results as effective in reducing injuries incident to automotive accidents. These include better positive lock doors, impact absorbent padding of dashes and sun visors, seat belts, collapsible steering wheels and posts, and other features of current models available to the public. Since the Armed Forces buy many standard model vehicles, these features will be phased into the military establishment through replacement procurement. In addition, the Assistant Secretary of Defense (Health and Medical) has instituted a positive approach to the adoption of seat belts in appropriate military vehicles.

The report on "Human Factors in Highway Transport Safety" has been published under the sponsorship of the commission and of other associations.[7] The response to this and a related series of reports[4-6] on highway safety and human-body size and capabilities in relation to vehicular design has been enthusiastic. Requests for copies were so numerous that additional printing became necessary. Comments from manufacturers indicate that the data are being used by the designers of all types of vehicular equipment and by safety personnel.

RESULTS

The Department of the Army motor vehicle safety activity is a continuing program which is steadily showing its effectiveness in a concrete manner. In 1955, motor-vehicle deaths involving military personnel driving their privately owned cars and man days lost due to accidents in privately owned vehicles were each *reduced 11 per cent*, and the direct cost of injuries and death *reduced 7.5 per cent* or an estimated saving of $1,040,000 over the costs of the previous year—1954. In addition, the Army motor vehicle *accident and fatality rates were reduced 7 per cent.* These declining figures definitely reflect safer operation of vehicles in the community. However, the cumulative effect of these activities must be measured not alone in reduced motor vehicle accident and fatality rates for the Army but in its beneficial effect on the nation's traffic-accident problem and, therefore, the nation's economy.

Based on current induction figures, reenlistments and separations, it must be assumed that a large portion of the male youth of the country has been or will be, in the foreseeable future exposed to the various elements of the Army motor vehicle safety program. They will have a keener appreciation of the magnitude of the traffic-safety problem; they will be more aware of their responsibilities as motor-vehicle drivers; they will be better informed concerning their limitations as drivers and the measures that they must take to compensate for their deficiencies; they will have a better conception of what constitutes a safe vehicle; they will be more proficient in the handling of motor vehicles and, therefore, better qualified to

meet traffic emergencies; and they will have a fuller appreciation of the importance of a unified effort in the community accident prevention program.

SUMMARY

Motor-vehicle accidents are a major cause of manpower loss to the military from non-battle injuries. *Prevention is the most remunerative approach to the problem.* The military commander is responsible for this activity at all echelons. Command emphasis has been applied from the civilian Secretaries of the Department of Defense and the military departments and the military heads of those departments.

Prevention is based upon positive measures of driver selection, training and retraining; traffic control; research and development to reduce or minimize causative factors; transportation control and supervision; and other measures. Like the maintenance of health, the maintenance of an effective accident-prevention program is dependent upon the individual in large measure. Educational and supervisory programs must be aimed at the individual.

Motor accident prevention activities in the Army are carried on by concerted and integrated action on the part of many staff agencies of the Commander. Command action puts the program over. The Army Safety Program is producing positive results in the reduction of motor vehicle accident rates because of these features.

REFERENCES

1. Cohen, S. A.: Accidents in the Army and their prevention, Mil Surgeon 87:434-443, 1940.
2. Fineberg, M. H.: A survey of the accidents resulting from Army maneuvers with recommendations for their prevention, Mil. Surgeon 91:75-81, 1942.
3. Health of the Army, Office of the Surgeon General, United States Army, 8:25, August, 1954
4. McFarland, R. A., Damon, A., Stoudt, H W., Moseley, H. W., Dunlap, J. W., Jr., and Hall, W A.: Human Body Size and Capabilities in the Design and Operation of Vehicular Equipment, Cambridge, Mass., Harvard, 1953 (revised 1954).
5. McFarland, R. A, Dunlap, J. W., Jr., Hall, W. A., and Moseley, A L.: Human Factors in the Design of Highway Transport Equipment: A Summary Report of Vehicle Information, Cambridge, Mass., Harvard, 1953.
6. McFarland, R. A., Moore, R. C., and Warren, A. B.: Human Variables in Motor Vehicle Accidents, Cambridge, Mass., Harvard, 1955.
7. McFarland, R. A., and Moseley, A. L.: Human Factors in Highway Transport Safety, Wakefield, Mass., Murray Printing Co., 1954.
8. Manual on Uniform Traffic Control Devices for Streets and Highways, Public Roads Administration, Federal Works Agency, Washington 25, D. C., U. S. Government Printing Office, 1948 (with revision supplement of 1954).
9. Medical Statistics of the United States Army, Annual Report of The Surgeon General, Calendar Year 1953, Frontispiece —Admissions for Disease and Non-Battle Injury, U. S. Army, 1819-1953, Washington, D C., U. S Government Printing Office, 1955.
10. *Ibid.*, Chart 1, p. 23.
11. *Ibid.*, p 27.
12. Preventive Medicine in World War II, vol. 3, Medical Department United States Army, in World War II, pp. 237-238, Office of The Surgeon General, Department of the Army, Washington 25, D. C., U. S. Government Printing Office, 1955.
13. *Ibid.*, p. 238.
14. *Ibid.*, p. 239.
15. *Ibid.*, pp. 239-241.
16. *Ibid.*, pp. 241-243.
17. Staff Officers' Field Manual, Staff Organization and Procedure, Department of the Army Field Manual 101-5, p. 4, Washington, D. C., U. S. Government Printing Office, 1954.
18. *Ibid.*, p. 13.
19. *Ibid.*, pp. 26-28.
20. *Ibid.*, pp. 31-32
21. *Ibid.*, p. 37.
22. *Ibid*, pp. 37-39.
23. Thacher, J.: A Military Journal During the American Revolutionary War from 1775 to 1783, Boston, Richardson and Lord, 1823.
24. Uniform Vehicle Code, Washington, D. C., National Committee on Uniform Traffic Laws and Ordinances, revised 1954.

9

The Role of Safety Belts in the Motorist's Safety

ANDREW J. WHITE*

The amazing progress of science and technology in our time, which has endowed mankind with virtually unlimited physical power, has brought with it a gigantic responsibility. Achievements such as the mobile power of the internal combustion engine, the conquest of geographical barriers by the aeroplane, the boundless communications made possible by electronics, and now atomic fission with all its ramifications have provided the means of performing miracles and producing catastrophes.

—DE FLOREZ

Many critical studies of the average human being have been made. The subject obviously is a complex one that involves psychology, physiology, mechanics and even spiritual forces, of which we yet know little. These studies represent only a beginning and a continuing and ever-expanding compilation of data that will provide the planner and the designer with the probable characteristics of the average individuals who will man our machines of the future—an absolute necessity for survival.

It is indeed unfortunate that our technologic advances have been so rapid without complete consideration of the human capabilities. This is what has happened when one relates the modern automobile and its operating characteristics to the accidents and trauma on our highways.

In the last analysis, all accidents are due to human failures. Let us take an extreme case! A car blows up because there has been an explosion in the gasoline tank. The human element has failed because of the omission to replace the fuel filler cap, thus permitting air to enter the tank and form an ignitible mixture. Plainly, perfection cannot be approached by human beings, and accident prevention becomes largely a matter of making it physically impossible for human beings to fail in certain dangerous ways.

---

*Director, Motor Vehicle Research, Inc., So. Lee, New Hampshire.

(The reader was warned at the beginning of this symposium that we were in a state of transition with regard to motorist safety and that, therefore, the last word had not been said, especially with regard to supplementary methods. Mr. White, of Motor Vehicle Research, Inc., is currently engaged in studies with regard to safety-restraining devices (under contract with the Air Force). His chapter is to the point and is written with his usual vigor. It is extremely thought provoking. The editor has been advocating safety restraint for some time He feels that the sooner we find out our mistakes the sooner we can rectify them. In other words, the safety belt is better than no restraining barrier at all. That has been my opinion from the first in this regard. After reading Mr. White's ideas it will be evident that at long last real progress is being made along this simplest of all principles—safety restraint.

Mr. White's remarks illustrate another point which has been stressed in this symposium—the interlocking relationships that exist between medical and engineering aspects of this problem His interest in and apparent understanding of the former is most welcome, and stated strikingly.

This chapter rightfully belongs in the previous number of *Clinical Orthopaedics*. However, Mr. White wished to make further observations in regard to safety restraints before presenting his present argument. The reader will agree that our extension of time to Mr. White is fully justified [Ed.])

One example is the separation of opposing lanes of traffic to prevent motorists from indulging in head-on collisions.

While the automotive industry has a very direct responsibility to those who purchase automobiles, up to the moment it has given very little consideration to safe design modification of the vehicle that would result in some protection to the passengers in the event of a mistake in operation. There is no question that automobiles can be made safer in the event of an accident. Despite this, some recent models have been styled and furnished inside without sufficient regard for simple safety considerations. Yet the performance ability of most modern vehicles has been steadily increasing to a point where control becomes ever more difficult by the average man under some operating conditions. While it is true that over the past years valuable features have been introduced to minimize component failures that undoubtedly would end in injury or death to the operators of these vehicles, we cannot wholly construe these features as safe design modification The introduction of four-wheel brakes might be mentioned under this heading, although we cannot be concerned here entirely with technical innovations.

Considering the performance characteristics of our automobiles over the past 10 years, we have seen a steady increase in this area. Yet these same automobiles are incapable of providing passengers with even the minimum protection in the event of a fixed-object low-speed collision. Recently buyers have been offered various safety modifications by several manufacturers which now are proving to be token offerings rather than a direct approach to the problem based on experience and basic laws of physics It is very difficult to understand the motivating forces that prompt individuals and agencies to use any particular series of events to indicate a trend without considering all controlling factors. For example, there was widespread editorial treatment of the fact—latter 1955 and early 1956—that a greater number of miles were being covered by more automobiles with no increased rate in injury or death. Suddenly there was a very substantial increase in motor vehicle accident injuries and deaths. Yet a corresponding increase in mileage was not present. Perhaps, in the first instance, too little consideration was given to the medical profession for preventing deaths by means of new drugs, technics, etc. *It now appears that the rate of increase in injuries and deaths suddenly became greater because the facilities of the medical profession were overtaxed.* This seems to be true in spite of the fact that to a large degree the medical profession has advanced faster in the last 25 years than any other science. Briefly, we might say that the increased use of the automobile by the average man, together with increased performance characteristics, has resulted in an increase in injury and death in spite of the valuable accelerated efforts of the medical profession. This particular phenomenon might be likened to a man's attempting to bail out a well whose input of water was greater than the man's ability to remove the same in a given length of time.

With this increase in accident trauma, many individuals, including the manufacturers of automobiles, have hastened to adapt hang-on safety features to an obsolete vehicle from a standpoint of protection in the event of a crash deceleration. Thus, automotive seat belts currently offered as optional equipment by car manufacturers and others clearly indicate that a need exists for car-occupant restraining devices. Ultimately the true value of these devices to protect car occupants in crash decelerations will be found from a study of thousands of case histories of accidents in which belts were used On this basis the true value of restraining devices may not be discovered for many years. Fortunately, there are available data of a significant nature dealing with seat belts and restraining harnesses used by human beings during aeroplane crashes, which can serve as a guidepost for future investigators. Some of these studies indicate that seat belts have a limited ability to pro-

tect occupants in crash decelerations of certain magnitudes and impact angles. There is a substantial amount of evidence that clearly defines the protective qualities of seat belts, even though these qualities are limited and are operative only under certain conditions. Other studies show the inherent lack of protection and injury-producing qualities of seat belts in some circumstances. *Somewhere in between lies the answer to the true value of seat belts as safety devices.*

Considering the dynamic effects of impact forces when applied to a complex elastic system such as the human body, all test devices, including anthropometric and anthropomorphic dummies (Fig. 16), have limited value in research fields dealing with restraining devices. Dummies serve as a guide for the time-motion histories of a mass during a deceleration but fail to respond to dynamic forces in the same manner as the human body. Most studies of seat belts and harnesses employing simulated human bodies cannot be considered wholly valid when the human body is basically what is under study.

The differentials found in the interior environments of present-day automobiles might cause some investigators to report a seat-belt installation the primary reason for passenger protection, *when some other factor contributed a large percentage of this protection in combination with the seat belt.* Differentials in impact angles of the same vehicle can confuse investigators and might lead to the abandonment of restraining devices now under consideration or to the limited use of them.

Present data indicate the limited value of seat belts and should be given consideration. This limited work is intended to show the variables encountered in automobile-accident investigation and may assist in pointing out features generally overlooked when seat belts are evaluated at accident scenes.

CRASH DECELERATION

The rapid and ungoverned dissipation of the vast amount of kinetic energy a vehicle



FIG. 16 Anthropometric and anthropomorphic dummy used by M.V.R. to study kinematic behavior of a human being during a crash deceleration.

possesses at high speed usually results in extensive structural deformation and death and serious injury to the occupants of the vehicle in a crash deceleration.

Preventing the collapse of the structure surrounding car occupants and restraining them from contacting this surrounding structure is a direct method of reducing the highway toll of human life. Structural collapse (Fig. 17) includes the prevention of the opening of doors in all types of accidents. Large factors of safety are basic principles of engineering and can be built into our automobiles.

DESIGN CONSIDERATION

The design and the installation of restraining devices such as seat belts require consideration of the many force-angle fac-

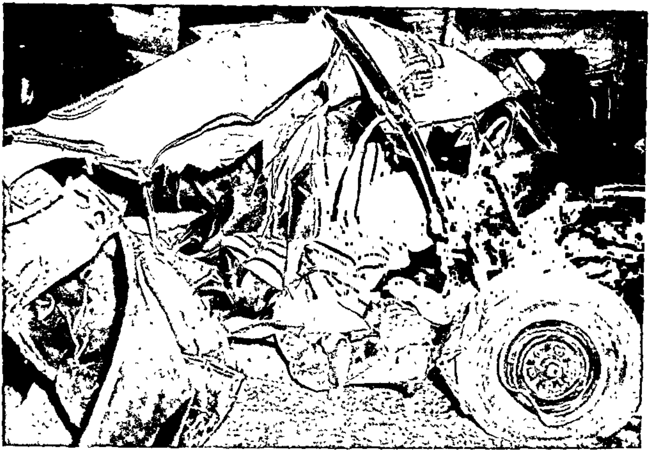


Fig. 17. Structure was incapable of withstanding (crash) forces, and passenger was badly crushed and died. Driver was ejected and received only minor scratches.

tors included in a crash deceleration. It is highly improbable that any one make of vehicle will impact objects in the same manner during a series of accidents. To a large degree the contact area of the impacted object will control the forces acting on vehicle occupants.

These forces are also controlled by time-distance relationship and sheet-metal deformation factors included in the deceleration.

Consideration should be given to the pre-impact position of the occupants, together with crash-awareness tension or the bracing of the occupants

It is known, also, that the forces acting on occupants in vehicles involved in fixed-object head-on types of crashes will be higher than those found in a two-vehicle crash. This is due to the fact that when two vehicles collide, one or both vehicles usually come to rest some distance from the initial point This distance (decelerative) tends to reduce forces acting on the occupants because the kinetic energy of the vehicles is dissipated over a longer period of time and over a greater distance. However, especially in multivehicular accidents of this type, occupants sometimes are subjected to radical changes in direction during the deceleration time because some peak-force intervals are acting upon them in many planes It is obvious, therefore, that restraining devices should be designed to cope with these variable forces within the limit of tolerance of normal and even subnormal riders.

INTERIOR ENVIRONMENT AND STRUCTURE

The severity of injury in automobile accidents is rarely in direct ratio to crash force. When vehicular body structure remains substantially intact, crash injuries are principally the result of the individual's being thrown against objects inside the compart-

ment. Wide variations in the extent and the severity of injury among several people who have been in the same crash are not uncommon. Variations often are due to the "injury potentials" (of interior design) of the objects which each person struck rather than the force of the crash.

REAR-PASSENGER BEHAVIOR DURING FIXED-OBJECT CRASH

It is difficult to predict kinematic behavior of rear-seat passengers during a fixed-object crash; it is dependent on many factors: angle of vehicle contact; area of impacted object; application of brakes prior to impact; and others.

Front-seat passenger wearing seat belt would receive energy of rear-seat passenger's weight less seat frictional losses of rear passenger in this type of crash. Rear-seat passenger, weight 87 lbs. (semiarticulated dummy anthropomorphic type). Force was sufficient to increase head blow of front passenger on dashtop and face, causing denting of metal area contacted. Additional abdominal load is impaired on front-seat passenger at belt area.

Front-seat back is hinged for entrance and exit of rear seat passengers. Force requirements to move seat back was negligible (static test).

Jackknife action of front-seat passenger would cause pressure point on abdominal area by buckle of seat belt.

NORMAL WEAR FACTOR OF WEBBING AT FLOOR ANCHOR POINTS

The design of floor anchor points of seat-belt assemblies should receive consideration. Some designs allow the shoes of rear-seat passengers to contact the web loop. Abrasive wear and deterioration from moisture and dirt carried into the compartment on the soles of footwear can cause webbing failure under loading.

Average motorists might not inspect belt assemblies and anchor points on a periodic basis to determine normal wear factor. Belt-webbing failure in crash may result. Design should include protection of floor anchors and webbing exposure to moisture, etc.

KINEMATIC BEHAVIOR OF PASSENGER IN CRASH

Unrestrained rear-seat passengers are acted upon by a vertical component of a crash, causing them to continue forward and upward. Restraint by means of a seat belt properly installed would reduce injury potential to some degree, provided that no head contact was made to a structural or high-pressure point.

HUMAN EXPOSURES TO LINEAR DECELERATION*

The Lap Belt. Assuming the usual width of 2 inches, the average occupant of an aircraft seat equipped with a lap belt will impinge against approximately 20 inches of its length across the anterior aspect of his trunk. In order that it can have any protective function against crash forces, the occupant must have at least 40 inches of forward clearance to avoid striking his head against obstructions as his trunk swings in an arc around the belt as a fulcrum; the belt must pass through the crease of the hips to avoid bearing against the abdomen, and the load must rest against all 40 square inches of presenting surface, not against an upper edge, or a doubled belt. Under these ideal conditions, the 200-pound occupant will sustain a load across his pelvis of 5 pounds per square inch per g. At 20 g, this is 100 pounds per square inch, and at 40 g it is 200 pounds per square inch. The maximum pressure listed in Table 2, Column K [not reproduced here], is 36.5 pounds per square inch under actual test conditions. While this is by no means the limit of tolerance, it would be rash to recommend more than three times this value as the extreme limit for the safety belt alone, operating under ideal conditions, such as in a laboratory. In actual practice, the occupant seldom is given 40 inches of unobstructed forward clearance in which to jackknife his body; the angle of application of force may pull him partly or completely out from under the belt, or impinge his lower abdomen along one edge or a doubled V of the webbing, or the belt

*Excerpt from AF Technical Report 5915, Part 2, December, 1951, by John Paul Stapp, Lieutenant Colonel, MC, USAF.



FIG. 18. Dashtop deformation by dummy's head after windshield penetration.

may catch under the margins of the ribs across the upper abdomen. The effect of 100 or 200 pounds per square inch in shear on these soft tissues and the organs underneath is almost certainly to rupture and tear.

FREQUENCY OF HEAD INJURIES IN ACCIDENT AND POSTACCIDENT COMPLICATIONS

Numerous statistical studies disclose the high incidence of fatal and nonfatal head injuries in automobile accidents. Medical data indicate that the dynamic energy input required to cause head fracture is much lower than the energy requirement of a static load to cause a similar fracture. *No significant data have come to light disclosing the contribution to death or mental complications that may result from a head blow received in an automobile accident many years before.* However in the field of boxing there is ample evidence of the postaccident complications that can occur when a blow or repeated blows to the head have been received. Since 1900, over 300 men have died from injuries incurred in the ring. No count of those who died months and years before they were buried is available. An article in *The Journal of the American Medical Association*, by Dr. Frank Ferlaino, shows the need for boxers' gloves so designed as to afford the hand less protection and the head more. In this respect the same consideration is needed in designing the automobile dashboard top and face and other surrounding structures that might be impacted by the head during a crash. This is imperative because seat belts will not restrain the upper torso in most crashes

Brain-wave tracings by Dr. Harry A. Kaplan and Dr Jefferson Browder, summarized in *The Journal of the American*

Medical Association, showed that only a few of the 1,000 boxers examined directly after a fight had the type of brain wave that might be termed *classic*.

Some human heads are more vulnerable to blows than others. Usually this is traced to the thinner frontal bone shielding the brain behind the forehead.*

The majority of solid blows to the head are apt to cause minute hemorrhages on the brain surface. It may take years for the effects of such hemorrhages to reveal themselves. Damage to the brain through hemorrhage or otherwise is irreversible. Unlike other parts of the body, the brain cannot repair itself.

It is probable that no head blow is taken with impunity. Unconsciousness from a head blow usually results in irreparable brain damage. [7]

Since protection for the head cannot be provided by seat belts (Fig. 18), internal structure design and proper restraint for the upper torso seem to be the logical approach. Injury to most other parts of the body, while crippling and disabling, have largely been circumvented by modern technology. Almost any damage to the body can be repaired by surgery, but damage to the brain cannot be repaired.

Because head blows dominate the list in automobile-accident injuries, it is well to consider the limited ineffectiveness of seat belts as a protective measure.

HEAD-INJURY CONSIDERATIONS

It can reasonably be concluded from statistics that head injuries predominate in most cases of death or injury to occupants of automobiles involved in crash decelerations Restraining the lower body by means of a seat belt alone will not reduce head injuries materially if the surrounding structure is within range of the head during a crash. High-pressure structural points would also increase the injury exposure materially.



FIG. 19. Side view of steering-wheel condition after impact by dummy.

Disregarding the crashworthiness of the car-body structure surrounding the occupants, which of course should be a primary consideration, *we must view the internal environment as an immediate source of injury potential* (Fig. 19). It is this source that should receive consideration when seat belts are involved, because of their interrelationship. Why restrain the lower-body section when the head is most vulnerable to impact? To restrain the lower body and allow the head to impact a knob or dash contour that will cause a localized high-pressure force to be transmitted to a body section so sensitive to injury seems to defeat the purpose of a seat belt.

Moderation of the mechanical causes of head injury is so closely related to seat-belt protection that it cannot be ignored. In some accident cases it might well be proved that a seat belt was the cause of death or injury. For example, a fixed object crash occurs at a relatively low speed. The passenger's body is restrained with a seat belt that functions properly within the limits of the forces involved. The upper part of the passenger's body jackknifes and his head strikes a narrow dash contour or knob with a force suf-

*Tests at the University of Cincinnati by Dr. Laurence B. Chenoweth.



FIG. 20. Specially designed harness under evaluation.

ficient to cause *an undetected brain hemorrhage.* He dies a month or a year later, although no damage was evident at the time of the accident. This injury condition may occur also were the head to strike a crash pad designed for protection at low-velocity impacts In the same crash without a seat belt this passenger might have impacted the same area or some other area with another part of his body less vulnerable to injury, or the force might have been distributed over a greater body area that would materially reduce the injury potential. The seat belt, therefore, could be the direct cause of death or serious injury. The answer obviously is not any kind of restraint!

Our studies indicate clearly that the modern automobile in a crash deceleration into a fixed object will not provide a passenger with any protection at impact speeds even as low as 13 miles per hour. These studies show clearly that the frontal area and structure composed of the grill, the fenders, the bumper, etc., absorb a minimum of the kinetic energy available when a car is decelerated by means of contact with a fixed object. Moreover, our studies clearly support prior studies in this particular area. While it is true that the sheet metal and grill area, etc., of the modern automobile absorb some energy, the percentage that it absorbs is negligible in protecting the passengers of the vehicle.

The immediate dangers to fliers from rapid deceleration resulted in the development of an effective restraining harness. This harness consists basically of straps that hold the body firmly in its seat, controlling both the upper "shoulder" and the lower "pelvis" portions of the body (Fig. 20). Previously, a simple lap strap was used, but this offered some protection in low-speed crashes only

and was found to be useless, if not dangerous, in high-speed crashes, because it permitted the spine to flex forward and allowed the head to strike the cockpit (jackknifing). Moreover, the snubbing action of a seat belt in very violent crashes may compress the soft organs of the abdomen, such as the liver and the spleen, which in certain circumstances could amount to rupture or pulping.

While our experiments have not covered the medical aspects of the injury potential of a seat belt, they have shown clearly that such a device has extremely limited protective qualities.

Our experiments with particular restraining devices being adapted to the present seat configurations have proved to be unsatisfactory. We may say that a satisfactory harness was designed, but difficulties were encountered when it was observed that, though the harness withstood the forces of deceleration, either the seat itself broke up or its fastenings to the floor became detached. Thus it was necessary to stress both the seat and its attachments to restrain forces at least equal to those which the harness was designed to meet. It was observed through a study of ultra-high-speed motion pictures that the present-day harness, even though anchored to the floor, depended upon the rigidity of the seat back in order to provide the wearer with a measure of protection.

Most harness assemblies installed in the modern automobile are anchored to floor pans or frame areas directly behind the back of the front seat. The shoulder harness is secured to this anchorage point and continues vertically to the top of the seat, then over the shoulder of the occupant and back down to the anchorage point. Should the back seat be stressed beyond its resistance qualities, this webbing line attempts to assume a straight line between the anchorage point and the contact point on the top of the seat back or the shoulder of the occupant. When the seat back fails, the distance between the dash and windshield area of the vehicle and the occupant becomes shorter and in most cases allows the occupant to contact these particular sections of the automobile.

It is apparent from our studies that the adaptation of any present-day harness or seat belt has many limitations. Our current data sum up the value of a seat belt in the following manner:

If it is possible to set up the type of accident in which a person wearing a seat belt is going to become involved, then it is desirable to wear such a restraining device. If this is not possible, the restraining device worn might be the direct contribution or the primary cause of injury or death.

A simple seat belt, a device very similar to that used in civilian passenger aircraft, can be adapted easily for all positions in the average car and offers the advantage of being inexpensive, can be fitted easily and worn with relative comfort over long periods. Although this seat belt offers some protection to rear passengers, both the driver and the front passengers are liable to injury due to jackknifing or the flexion action of the body or to being thrown forward, either over or under the lap strap in medium high-speed crashes. I feel that a seat belt cannot be recommended for these two positions, since it offers little or no protection to the head although it has been stated that the belt will reduce the amount of energy absorbed by the head.

A recent survey of safety groups, insurance companies, law-enforcement groups and others has disclosed definite divided opinion regarding the protective qualities of seat belts and harnesses in the modern automobile Should we assume for a moment that a seat belt or a restraining harness is effective in the modern automobile, provided that such devices are properly designed and produced to withstand certain dynamic loadings, we should then consider the quality and the design of a number of restraining devices now being offered to the public. On an ocean liner in continental

Europe it is required by law that boat drills be held, both for crew and passengers, within a very short time after the ship leaves port. All persons are required to present themselves at an allotted boat station wearing correctly a regulation life jacket. Perhaps the most vivid memory of these occasions is the sight of the very differently clad crew and passengers, *who, however, show a distinct uniformity of appearance because of the same type of life jacket,* a jacket that has proved its worth and whose use is mandatory by maritime officials.

It is with considerable wonder that a casual shopper sees a variety of seat belts and harnesses on sale in various shops at prices ranging from approximately $3.00 to $25.00 and all carrying claims of excellence in well-worn sales phrases. The analogy between life jackets and seat belts should be very close. Both are designed specifically to save life. However, in practice the analogy breaks down completely, for the former are demanded by law and are approved after testing, while serious doubts have been raised as to the efficiency of the latter, which do not have to meet practical or official specifications as to design or the materials used in their construction.

A restraining device is, or should be, a scientifically designed article produced with the clearest concepts in mind of what it has to do and how it is to do it. Consideration should be given to its particular adaptation to particular vehicles. Unfortunately, judging by the multitude of materials, and even the basic designs of restraining devices that are offered, it is abundantly clear that these concepts have been neither understood nor investigated, and, so far as officials are concerned, no practical law exists to ensure that even the minimum of safety is provided by a safety belt. A survey of the few laws regarding safety belts and test procedures for approval indicates that those directly connected with the creation of these laws have little or no conception of what a seat belt should provide in order to provide even the minimum of protection. Therefore, it is not surprising that *the public buys according* to its pocket, in sartorial fancy, acquiring all too often no more than an illusory protection, facts about which coroners recently have made pungent remarks when investigating fatalities on the road. This position then is rendered more tragic when it is remembered that the dead motorist bought this restraining device with the express idea of protecting himself from such a fate.

Several of our tests have shown that, with impact velocities below 30 miles per hour in a crash deceleration into another vehicle, the seat belt, which was standard and purchased on the open market, failed to restrain the dummy occupant of the vehicle used in the test. Further dynamic crash tests of the various types of seat-restraining devices should indicate clearly the effectiveness of such devices. Manufacturers have been explicit in their literature concerning restraining devices for children that these will provide protection and prevent injury even under most severe crashes. Such sales claims, influencing public thinking, are certainly a clear indication that the commercial aspects of human safety are more important than the basic concepts of it. How can we, then, openly endorse present-day restraining devices and even predict that these devices have protective qualities when the human tolerance to forces produced by crash deceleration are practically unknown?

There also have been numerous studies that indicate that prevention of ejection during crash decelerations of car occupants would reduce the number of killed or injured each year. *These studies are not valid in view of the fact that no data concerning the condition of the occupant of the vehicle are available immediately prior to the ejection.*

Our studies show that in a head-on type of crash the passenger continues forward, impacting the windshield or dash area prior to ejection. Is it not worth considering whether this particular passenger was in-

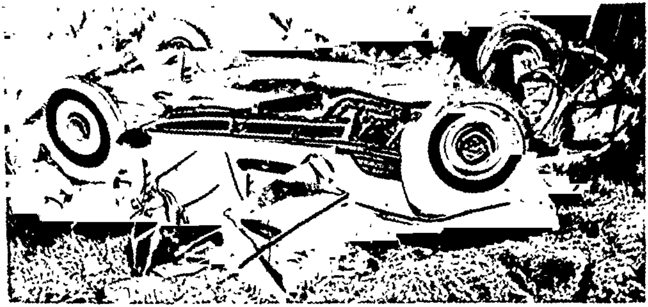


FIG. 21. Rest position of vehicle in roll-over.

jured critically or fatally prior to the ejection or whether the primary impact was a positive factor in death or injury and not contact with some external environment?

Our field studies at this time involving late-model vehicles show decisively that our present-day door locks are not safety door locks and provide little protection in most crashes.

Without question our roof structures are inadequate (Fig. 21), and we are fast accumulating valuable data from our studies in this particular area. In order to satisfy rock-bottom requirements for safety, a reinforced compartment must be provided that is a strong crash-resistant compartment that might be termed a *capsule for maximum occupant protection.*

Basically, up to this time we have not provided our vehicles with any crash design modification, and, unless such modifications are undertaken and incorporated in our vehicles, the accident trauma will continue at an accelerated rate until the automobile becomes the most lethal instrument ever produced by man. It is amazing that our technologic advances in automotive design can provide us with accelerations and top speeds of over 120 miles per hour, yet no provision for safety in the event of an accident is incorporated in the over-all design.

Editorial comment lauding the crash-worthiness design of an automobile only delays much-needed action and puts off until tomorrow what we should do today. During this time interval many thousands of people will be severely injured or killed, and this will persist until such time as public indignation is aroused and steps are taken to tackle the problem and demand safety designing in our vehicles.*

However fast our scientific research provides safety at certain velocities, we cannot hope to counteract successfully the increase in operating speeds of vehicles and in impact velocities. In other words, we may provide protection for passengers by means of design at impact velocities of 20 miles per hour while the designers of automobiles are contemplating an increased performance vehicle for the following year that will provide impact velocities of 75 miles per hour. *There must be a very close relationship between safe design modification engineering and performance engineering if we are to attack the problem and hold the line on injuries and deaths due to the accident trauma on our highways.*

A series of fixed-object crash-deceleration tests at impact velocities of 13.1, 14.3, 14.7,

* Total participation is needed. [Ed.]

Europe it is required by law that boat drills be held, both for crew and passengers, within a very short time after the ship leaves port. All persons are required to present themselves at an allotted boat station wearing correctly a regulation life jacket. Perhaps the most vivid memory of these occasions is the sight of the very differently clad crew and passengers, *who, however, show a distinct uniformity of appearance because of the same type of life jacket,* a jacket that has proved its worth and whose use is mandatory by maritime officials.

It is with considerable wonder that a casual shopper sees a variety of seat belts and harnesses on sale in various shops at prices ranging from approximately $3.00 to $25.00 and all carrying claims of excellence in well-worn sales phrases. The analogy between life jackets and seat belts should be very close. Both are designed specifically to save life. However, in practice the analogy breaks down completely, for the former are demanded by law and are approved after testing, while serious doubts have been raised as to the efficiency of the latter, which do not have to meet practical or official specifications as to design or the materials used in their construction.

A restraining device is, or should be, a scientifically designed article produced with the clearest concepts in mind of what it has to do and how it is to do it. Consideration should be given to its particular adaptation to particular vehicles. Unfortunately, judging by the multitude of materials, and even the basic designs of restraining devices that are offered, it is abundantly clear that these concepts have been neither understood nor investigated, and, so far as officials are concerned, no practical law exists to ensure that even the minimum of safety is provided by a safety belt. A survey of the few laws regarding safety belts and test procedures for approval indicates that those directly connected with the creation of these laws have little or no conception of what a seat belt should provide in order to provide even the minimum of protection. Therefore, it is not surprising that the public buys according to its pocket, in sartorial fancy, acquiring all too often no more than an illusory protection, facts about which coroners recently have made pungent remarks when investigating fatalities on the road. This position then is rendered more tragic when it is remembered that the dead motorist bought this restraining device with the express idea of protecting himself from such a fate.

Several of our tests have shown that, with impact velocities below 30 miles per hour in a crash deceleration into another vehicle, the seat belt, which was standard and purchased on the open market, failed to restrain the dummy occupant of the vehicle used in the test. Further dynamic crash tests of the various types of seat-restraining devices should indicate clearly the effectiveness of such devices. Manufacturers have been explicit in their literature concerning restraining devices for children that these will provide protection and prevent injury even under most severe crashes. Such sales claims, influencing public thinking, are certainly a clear indication that the commercial aspects of human safety are more important than the basic concepts of it. How can we, then, openly endorse present-day restraining devices and even predict that these devices have protective qualities when the human tolerance to forces produced by crash deceleration are practically unknown?

There also have been numerous studies that indicate that prevention of ejection during crash decelerations of car occupants would reduce the number of killed or injured each year. *These studies are not valid in view of the fact that no data concerning the condition of the occupant of the vehicle are available immediately prior to the ejection.*

Our studies show that in a head-on type of crash the passenger continues forward, impacting the windshield or dash area prior to ejection. Is it not worth considering whether this particular passenger was in-

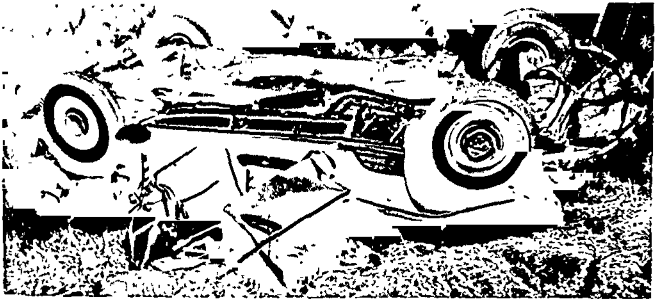


Fig. 21. Rest position of vehicle in roll-over.

jured critically or fatally prior to the ejection or whether the primary impact was a positive factor in death or injury and not contact with some external environment?

Our field studies at this time involving late-model vehicles show decisively that our present-day door locks are not safety door locks and provide little protection in most crashes.

Without question our roof structures are inadequate (Fig. 21), and we are fast accumulating valuable data from our studies in this particular area. In order to satisfy rock-bottom requirements for safety, a reinforced compartment must be provided that is a strong crash-resistant compartment that might be termed a *capsule for maximum occupant protection.*

Basically, up to this time we have not provided our vehicles with any crash design modification, and, unless such modifications are undertaken and incorporated in our vehicles, the accident trauma will continue at an accelerated rate until the automobile becomes the most lethal instrument ever produced by man. It is amazing that our technologic advances in automotive design can provide us with accelerations and top speeds of over 120 miles per hour, yet no provision for safety in the event of an accident is incorporated in the over-all design.

Editorial comment lauding the crash-worthiness design of an automobile only delays much-needed action and puts off until tomorrow what we should do today. During this time interval many thousands of people will be severely injured or killed, and this will persist until such time as public indignation is aroused and steps are taken to tackle the problem and demand safety designing in our vehicles.*

However fast our scientific research provides safety at certain velocities, we cannot hope to counteract successfully the increase in operating speeds of vehicles and in impact velocities. In other words, we may provide protection for passengers by means of design at impact velocities of 20 miles per hour while the designers of automobiles are contemplating an increased performance vehicle for the following year that will provide impact velocities of 75 miles per hour. *There must be a very close relationship between safe design modification engineering and performance engineering if we are to attack the problem and hold the line on injuries and deaths due to the accident trauma on our highways.*

A series of fixed-object crash-deceleration tests at impact velocities of 13.1, 14.3, 14.7,

* Total participation is needed. [Ed.]

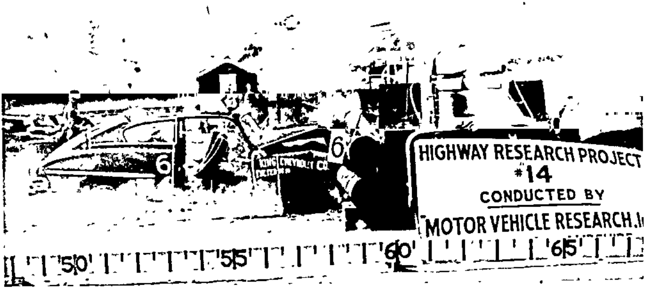


FIG. 22. Thirty-one milliseconds after contact was made.

15.4, 17.9, and 18.1 mph, using anthropometric and anthropomorphic dummies fully articulated and weighing 165 pounds, have provided valid data regarding the kinematic behavior of front-seat passengers wearing commercial seat belts.

A study of a motion-picture record of these tests recorded on 16 mm. film exposed at 9,000 frames per second revealed interesting data concerning the time-motion histories of the dummies and showed clearly that the front-end structures absorbed a negligible amount of energy by deformation. This plastic deformation absorbs much less energy than the elastic deformation of the vehicle mass that is present during a crash.

A reference fence positioned between the high-speed cameras and the crash vehicle provided a displacement record that was correlated with a time record made on the motion-picture film by means of a pulse generator. This generator supplied a pulse mark at the rate of 1,000 marks per second on a 400-feet roll of film.

The preimpact velocity of the vehicles and the deceleration rate of the dummies and the various sections of the vehicles have been studied by means of time-motion projectors These studies have shown the following:

1. Front end structure deformation absorbs a negligible amount of energy.

2. Elastic deformation is more effective in absorbing energy than plastic deformation.

3. Jackknife action of the passengers restrained with seat belts during a fixed object crash at 13.1 mph exposed the face and the head to violent deceleration by contact with the windshield and then caroming off to the dashboard top (Fig. 22). This condition existed even under an average deceleration of less than 6 g and does not consider several peak decelerations that occurred during the entire phenomenon.

4. The vertical components given to passengers in a fixed object crash at 13.1 mph are of a negligible nature and do not control the direction in which the passenger travels during a crash deceleration of this type at this velocity.

5. The coefficient of restitution of the vehicle at 13.1 mph impact was too small to have meaning.

6. Tests at somewhat higher impact speeds revealed factors not found at 13.1 mph. The vertical components given to the passengers were of a magnitude that controlled the direction of the passenger to a

large degree, and the coefficient of restitution was of a nature that warranted consideration.

7. Tests at 18.1 mph (preimpact velocity) using a standard nylon seat belt anchored to the frame of the vehicle and positioned across the lap area of the passenger at an angle of approximately 45° were ineffective in restraining the upper torso of the passenger. During the deceleration, the passenger remained in his preimpact seat position for 18 milliseconds, while the front end of the vehicle deformed. The velocity of the vehicle in the seat area did not diminish until the front-end deformation was almost complete and the nonyielding vehicle component of the mass was stressed. The passenger imposed a load on the seat belt that caused elongation of the webbing that reached an estimated 18 inches at one point in the deceleration. The head of the passenger penetrated the windshield approximately 7 inches. The elastic deformation of the windshield was considerable, yet the standard aluminum helmet was scarred and dented.

Knee-dash contact was present, and the head caromed to the dashtop, denting it approximately ⅞ of an inch over a wide area.

These actions were followed by a vertical rise of the passenger's entire body approximately 11 inches from the top of the seat squab until the body was almost horizontal with the head, near the center of the rear-compartment area above the seat back top. This action was followed by a one half cycle of the first action before the passenger came to rest in relatively the same seating position he occupied before the impact.

Although no attempt to relate the various forces involved in passenger injury was undertaken, due to the lack of valid data concerning injuries that actual human beings have received in this type of deceleration, it was concluded subjectively that the passenger was fatally injured. This conclusion was based on data that indicated that 400-inch pounds is sufficient to cause fracture to some human skulls, and any force above 600-inch pounds is sufficient to cause irreparable damage.



FIG. 23. Popular restraining seat for children used in collision tests (M.V.R.) with ¼-ton truck (collisions).

Another test at 17.9 mph using the same dummy showed that the large chest area of the dummy made contact with the dashboard face and reduced the head contact to the windshield and dashtop. The vertical component was reduced, and the dummy did not assume a horizontal attitute at any time during the deceleration.

This study clearly indicates a need for further investigation of seat belts before any valid conclusions can be reached regarding their usefulness. These studies now are under way, and a detailed report will be available sometime during the early part of 1957.

A series of crash tests of an exploratory nature have been made using various restraining devices for small children (Fig. 23), and results to date show a need for immediate full-scale investigation of these

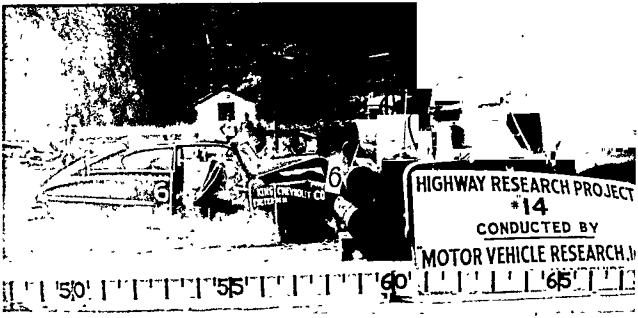


FIG. 22. Thirty-one milliseconds after contact was made.

15.4, 17.9, and 18.1 mph, using anthropometric and anthropomorphic dummies fully articulated and weighing 165 pounds, have provided valid data regarding the kinematic behavior of front-seat passengers wearing commercial seat belts.

A study of a motion-picture record of these tests recorded on 16 mm. film exposed at 9,000 frames per second revealed interesting data concerning the time-motion histories of the dummies and showed clearly that the front-end structures absorbed a negligible amount of energy by deformation. This plastic deformation absorbs much less energy than the elastic deformation of the vehicle mass that is present during a crash.

A reference fence positioned between the high-speed cameras and the crash vehicle provided a displacement record that was correlated with a time record made on the motion-picture film by means of a pulse generator. This generator supplied a pulse mark at the rate of 1,000 marks per second on a 400-feet roll of film.

The preimpact velocity of the vehicles and the deceleration rate of the dummies and the various sections of the vehicles have been studied by means of time-motion projectors. These studies have shown the following:

1. Front end structure deformation absorbs a negligible amount of energy.

2. Elastic deformation is more effective in absorbing energy than plastic deformation.

3. Jackknife action of the passengers restrained with seat belts during a fixed object crash at 13.1 mph exposed the face and the head to violent deceleration by contact with the windshield and then caroming off to the dashboard top (Fig. 22). This condition existed even under an average deceleration of less than 6 g and does not consider several peak decelerations that occurred during the entire phenomenon.

4. The vertical components given to passengers in a fixed object crash at 13.1 mph are of a negligible nature and do not control the direction in which the passenger travels during a crash deceleration of this type at this velocity.

5. The coefficient of restitution of the vehicle at 13.1 mph impact was too small to have meaning.

6. Tests at somewhat higher impact speeds revealed factors not found at 13.1 mph. The vertical components given to the passengers were of a magnitude that controlled the direction of the passenger to a

large degree, and the coefficient of restitution was of a nature that warranted consideration.

7. Tests at 18.1 mph (preimpact velocity) using a standard nylon seat belt anchored to the frame of the vehicle and positioned across the lap area of the passenger at an angle of approximately 45° were ineffective in restraining the upper torso of the passenger. During the deceleration, the passenger remained in his preimpact seat position for 18 milliseconds, while the front end of the vehicle deformed. The velocity of the vehicle in the seat area did not diminish until the front-end deformation was almost complete and the nonyielding vehicle component of the mass was stressed. The passenger imposed a load on the seat belt that caused elongation of the webbing that reached an estimated 18 inches at one point in the deceleration. The head of the passenger penetrated the windshield approximately 7 inches. The elastic deformation of the windshield was considerable, yet the standard aluminum helmet was scarred and dented.

Knee-dash contact was present, and the head caromed to the dashtop, denting it approximately ⅞ of an inch over a wide area.

These actions were followed by a vertical rise of the passenger's entire body approximately 11 inches from the top of the seat squab until the body was almost horizontal with the head, near the center of the rear-compartment area above the seat back top. This action was followed by a one half cycle of the first action before the passenger came to rest in relatively the same seating position he occupied before the impact.

Although no attempt to relate the various forces involved in passenger injury was undertaken, due to the lack of valid data concerning injuries that actual human beings have received in this type of deceleration, it was concluded subjectively that the passenger was fatally injured. This conclusion was based on data that indicated that 400-inch pounds is sufficient to cause fracture to some human skulls, and any force above 600-inch pounds is sufficient to cause irreparable damage.



FIG. 23. Popular restraining seat for children used in collision tests (M.V.R.) with ¼-ton truck (collisions).

Another test at 17.9 mph using the same dummy showed that the large chest area of the dummy made contact with the dashboard face and reduced the head contact to the windshield and dashtop. The vertical component was reduced, and the dummy did not assume a horizontal attitute at any time during the deceleration.

This study clearly indicates a need for further investigation of seat belts before any valid conclusions can be reached regarding their usefulness. These studies now are under way, and a detailed report will be available sometime during the early part of 1957.

A series of crash tests of an exploratory nature have been made using various restraining devices for small children (Fig. 23), and results to date show a need for immediate full-scale investigation of these

devices, especially those sold bearing a guarantee of safety in the event of a crash. In these exploratory tests, all seven devices failed to provide even the slightest protection in a fixed object crash at 8 to 14 miles per hour.

Our field investigations of actual accidents now indicate that a large number of both passengers and drivers survived because they were ejected from the vehicle. This is in direct conflict with some studies but tends to question the validity of some subjective data used in those studies.

In a number of accidents the passengers and the drivers were ejected and survived, while those who remained in the vehicle received fatal injuries. Conversely, some people who were ejected died, but we were unable to determine whether or not they received fatal injuries prior to ejection or by contact with some external environment.

The problem is one of obtaining an abundance of valid data before a conclusion can be reached. In the meantime it would be most desirable to delete publication of questionable data and the advocation of seat belts in the absence of data that cannot be challenged.

Some of our studies of passenger behavior during fixed-object crashes at low-impact velocities have revealed interesting data and lead us to the conclusion that preimpact seating position of vehicle occupants, the angle of attack of the decelerated vehicle, crash-awareness tension of the passenger and the impact velocity of the vehicle control the kinematic behavior of such occupants. *Prediction of this behavior, even under controlled conditions, is not possible when a slight change in one condition occurs.* This change affects all other conditions to varying degrees, and it is impossible to predict the effect of these changes.

Our investigation included the mounting of a high speed missile camera on the framework attached to the rear section of various automobiles. This camera recorded the actions of occupants wearing seat belts during fixed-object crashes and collisions with other vehicles and trucks. No two time-motion histories could even approach uniformity; in fact, the differences were so widespread that no prediction of passenger behavior could be made even if the angle of attack, preimpact seating positions and many other factors were almost identical. This tends to support my theory that accident analysis studies reported are defective to some degree.

The most important consideration concerning seat belts used in automobiles is that data regarding these safety devices be valid and capable of withstanding investigation by further research. Until such data are to hand, all research groups should refrain from advocating such devices.

10

Concluding Opinions: Some Orthopaedic Aspects of Motor-Vehicle Accidents

JACOB KULOWSKI, M.D.

Orthopaedic aspects—like those of medicine in general—of motor-vehicle accidents are inextricably related to the extraclinical factors that govern the causation and results. Stated in chronologic order, the integrated clinical life history of motoring comprises preclinical, paraclinical, clinical and post-clinical phases.

PRECLINICAL: ACCIDENT PREVENTION

Properly any orthopaedic inquiry into fundamental etiologic patterns of accident causation must consider one chief parameter —the motorskeletal fitness of drivers. A degree of correlation between physical diseases and accidents was deduced from the high incidence of spinal arthritis in a series of residual neck and low back disabilities that resulted from motor-vehicle accidents.*

Approximately 50 per cent of these persons were found to have had varying degrees of cervical and lumbar arthritis (osteoarthritis for the vast majority). Drivers with spinal arthritis of the cervical region were more prone to rear-end and angular types of impacts, especially those that occurred at intersections, etc., than were those without cervical arthritis. To a lesser extent the same thing was noted with regard to lumbar arthritis. This was assumed to have been due to some limited peripheral vision incident to loss of rotatory (and other) movements of the arthritic spines.

By implication it may be deduced that other physical conditions that tend to interfere with the dynamic requirements of driving may cause greater-than-average accidents. This dynamic concept regarding riders other than guest passengers (drivers), who sit more or less statically (and relaxed), needs further exploration and development. To the many human variables already known, another has been added.

PARACLINICAL

PATHOGENESIS, INJURIES

This phase of the situation has focused attention upon equations between human tolerances to decelerative and/or accelerative forces and injury potentials of the vehicle (Fig. 24) Stapp has defined human tolerance as the limit of reversible incapacitation (approximately 50 g's when properly suspended). Accident configuration is largely a function of the initial and/or principal impact (Fig. 25). The repetitive nature of the impacts and patterns of injury would seem to impugn force magnitudes no less than design factors of the vehicle. But the direction of forces is nowhere better illustrated than in the rear-end types of collisions (Fig. 26). On the clinical side, in the series

*Author's series of 230 cases with 275 lesions Observed from 1947 until July, 1956 During the same period there were 375 cases with motor-skeletal injuries (458 injuries) The spinal series comprised about 65 per cent of the total number

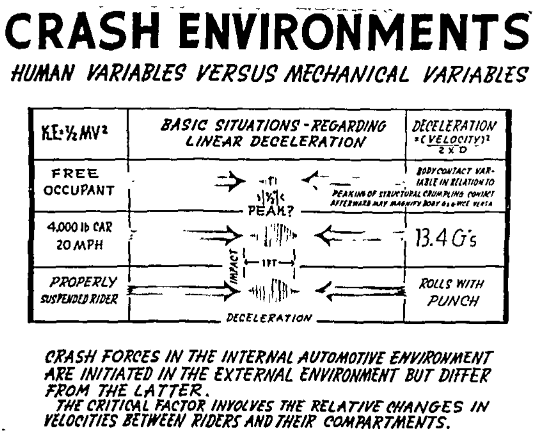


Fig. 24. Basic situations in automotive environments: suspended rider rolls with the punch.



Fig. 25 Practical results in automotive environments: central forward impact with tree Comminuted fracture of the femur resulted from knee-dash impact (pointed out by arrow).

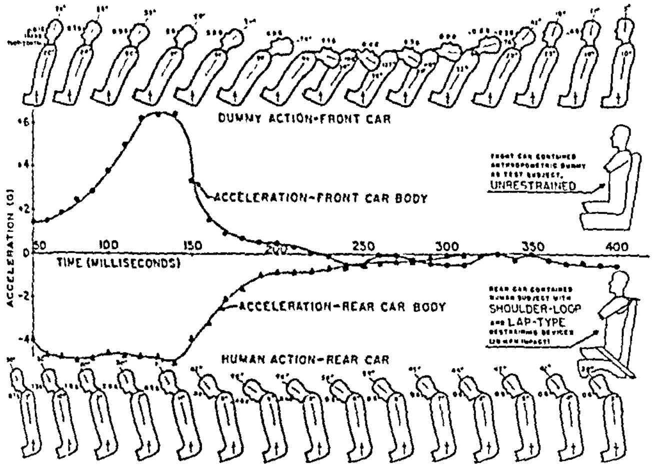


FIG. 26. Reactions in forward and rear impacting vehicles in experimentally controlled rear-end collisions. (Severy, Derwyn M., *et al.*: Controlled automobile rear-end collisions, Canad. Serv. M. J. 11:727)

of cases already mentioned with respect to spinal injuries, it was also found that the vast majority of so-called sprains (and some gross skeletal injuries) of the neck—and the low back—were caused by rear-end and angular impacts. However, all kinds of accident configurations may give the same results clinically. For this reason, engineering safety design takes cognizance of all available approaches to the reduction of injuries under crash conditions. In other words, the various kinds of forces operative are counterbalanced in one way or another (Fig. 27) in so far as they can be moderated in their actions upon the rider.

A. J. White (MVR) has also suggested marginal plantings of high energy absorbing shrubbery at strategic points on the highway.

The introduction of safety belts may pose some diagnostic problems (Fig. 28). On the other hand, another driver wearing a safety belt in a stock car race, in which his

TABLE 7. PRINCIPLE OF COUNTERBALANCE

FORCES ACTING ON RIDER	PRINCIPAL INJURIES	COUNTERFORCES THROUGH ENGINEERING
Impulsive	Fractures	Energy-absorbing surfaces
Crushing	Internal	Stiffen body of vehicle
Inertial	Internal and sprains	Controlled deformation
Combined (ejection)	Internal and fractures	Restraints; door locks

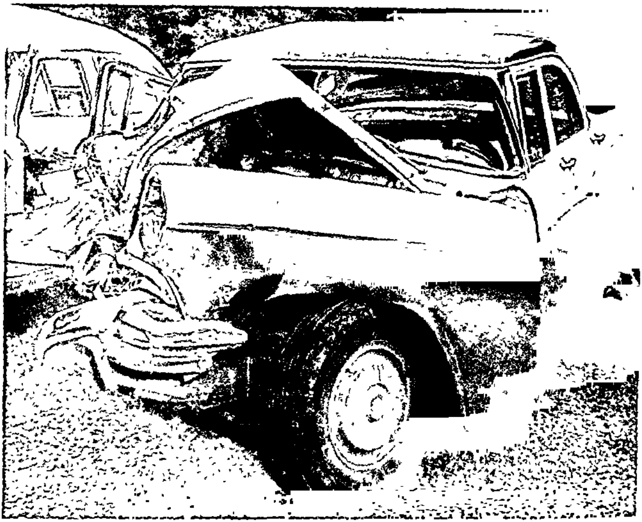


FIG. 27. Severe forward crash of 1956 model car Driver received injuries to right hip (dislocation), right arm, face, scalp and chest. Lifeguard steering wheel is seen to have withstood the driver impacts, although it was cracked in three places.



car rolled several times, received only a lumbosacral sprain, despite his increased vulnerability to low back injury due to the presence of a spondylolisthesis (Fig. 29). Be that as it may, much remains to be done along lines of reduction of injuries

The case mentioned above (Fig. 29) introduces a crash-impact point of view in reverse, i.e, connections between physical diseases (or conditions) and incidence of greater-than-average injuries (increased vul-

FIG 28. Abdominal adhesion from snubbing action of safety belt worn during panic braking and severe forward vehicular collision ([illegible] 3 months after injury). Operation [illegible] the chronic partial [illegible] inal o[illegible]

nerability). The 230-case series already mentioned with spinal injuries also showed many concurrent or accessory diagnoses (spinal and extraspinal), of which arthritis was the critical factor. There can be no doubt that many severe clinical reactions to accident configurations relatively moderate in scope were contributed to by the complicating spinal arthritis.

First Aid

The rules of the road in this respect have been motivated by humanity, sponsored by humanity, and sustained by humanity. Moreover, for the most part their execution is carried out by laymen. Orthopaedic surgeons can help to improve first aid in the following ways: they can speak against conversion of simple fractures to compound ones through poor handling (with or without splinting); they can work toward improving fracture splinting; and they can even accompany severe fractures to x-ray departments in order to instruct hospital personnel in the proper handling of these victims.

Rules of the Road

1. Remove victims from wreckage.
2. Keep the severely injured on the side for easier breathing.
3. Apply clean dressings.
4. Apply tourniquet only for brisk bleeding that cannot be controlled by simple compression dressings.
5. Splint obvious fractures of the lower extremity.
6. Use sling for fractures of the upper extremity.
7. See that transport to physician and/or hospital is rapid (safe).

CLINICAL

Emergency Care

The basis of emergency care is derived from the concept of primary shock. It has been augmented by the concept of secondary shock (Fig. 30). The clinical implications were noted in 19 fatalities (*with postmortem*

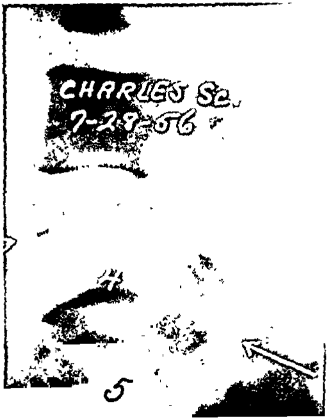


Fig. 29. This wearer of safety belt in multiple roll-over suffered only a moderate lumbosacral sprain despite the predisposing congenital lesion to more than average injury. Also notable was evidence of old injury to L-4.

studies). Ten died from primary shock within a few hours after admission to the hospital; 9, from secondary shock within 48 hours afterward:

Table 8

Primary Internal Injury	Primary Shock	Secondary Shock	Total No. Who Died
Chest	7	6	13
Head	4	9	13
Abdomen	3	3	6
Massive hemorrhage	5	3	8

It is helpful to recall (from Section I) that the ranking severity of injury involves the chest in the early stages after accidents. The head gains ascendancy a little later due to the space occupying complications. The delayed effects of hemorrhage are gaining



FIG. 30. Classic example of delayed death from secondary shock (about 10 days after admission with severe multiple injuries) despite adequate airway. Microscopic examination showed fibrinoid emboli in the lungs (thought clinically to have been an aspiration pneumonia); and kidneys (collagen reaction?); and an infarction of the pituitary gland.

attention A persistent low red blood count and other signs of anemia may spell varying degrees of nephrosis. The major complication noted in 30 fatalities was: hemorrhage, 66 per cent; all others, 34 per cent. Secondary or indirect complications included: infections, 39 per cent; pulmonary, 25 per cent; embolic, 16 per cent; nephrosis, 6 per cent; and degenerative states, 4 per cent.

Open Airway to Survival. The limits of factors of safety of the human body are best exemplified by the small airway at the glottis. But the ensuing pulmonary embarrassment results most often from disturbed physiology of the chest and pulmonary ventilatory system from painful splinting because of blood, fluid or air in the pleural cavities or from a shifted or shifting mediastinum.* In some of these people, tracheotomy—with or without other local measures (usually, but not always, in the domain of the thoracic surgeon)—may be lifesaving, even when *in extremis* and death rattle.

The results of the insertion of the tracheotomy tube are very dramatic (Fig. 32), but the best results are obtained during stages of hypoxia, not anoxia (elective insertion versus emergency insertion). Tracheotomy is a simple procedure; it is done easily at the bedside when necessary, but it is effected most comfortably in the operating room.

It may be necessary to decide between tracheotomy and intermittent (or other) positive pressure breathing. This should be left to the judgment of an internist (when available) if time permits.

In any case, a poor response to a tracheotomy performed judiciously should alert one

*Relief of tension pneumothorax is best done through aspiration with a thoracotomy tube. Mediastinal emphysema is detected by needle aspiration in the second or the third interspace next to the sternum and pointing the needle medialward. Tracheotomy may reduce the "dead" space in the respiratory passages by 50 per cent or more, allowing decrease in tidal air but enough for provision of adequate oxygen.

TABLE 9. DICHOTOMY OF EMERGENCY CARE (FIG. 31)

MEDICAL RESPONSIBILITY	HOSPITAL RESPONSIBILITY
Arrest bleeding	Provide tools, space and personnel
Provide adequate airway	Render first aid
Treat primary shock	Provide blood, plasma, plasma expanders
Sedation (?)	Provide electrolytes
Check urinary bladder for injury	Provide adequate x-ray facilities
Splint adequately or apply traction	Institute routine laboratory tests
Determine therapeutic priorities	Provide gentle intramural transport



FIG. 31. Unusual compound protrusion of the lower end of the femur due to severe shearing forces exerted on the fixed leg (closed kinetic chain?) during a forward vehicular collision and knee-dash impact. Compound fractures fall naturally into the domain of orthopaedic surgery.

to look for the cause in the mediastinum or in the lungs themselves.

DEFINITIVE DIAGNOSIS/TREATMENT

From the standpoint of survival the orthopaedist is involved to the same extent as are other members of the team who undertake to treat the severely and dangerously injured riders. The critical factors, of course, are: the internal injuries; immediate and delayed complications and reactions to operative and medical treatment. These untoward reactions to treatment—especially surgical—have not been adequately appraised. On the other hand, surgical treatment was withheld due to missed diagnosis in some cases; for example, those with severe mediastinal lesions (Fig. 33). In retrospect it is evident

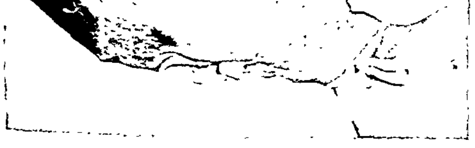


FIG. 32. The open airway to survival—but in this case see Figure 30, same case.

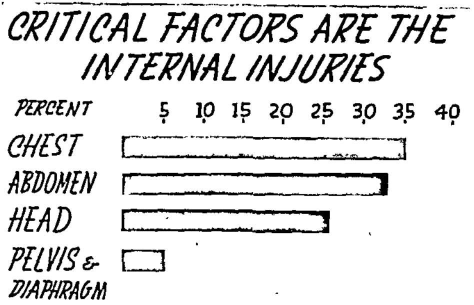


FIG. 33. Frequency rates of primary internal injuries noted at autopsy in a series of 29 subjects (based on injuries, not cases).

that not infrequently this was due to a mistaken idea that these patients were too ill to risk movement to x-ray, where fluoroscopic examination would have substantiated the tentative diagnosis of mediastinal injury, especially injury that interfered with cardiac action It cannot be done with inadequate portable x-ray films. Fluoroscopic inspection is required for the detection of pericardial and other injuries of the heart and great vessels. It can be stated almost axiomatically that no patient is too critically injured for diagnostic manipulations that may be lifesaving. However, most acute injuries of the motorskeletal system present problems of treatment and management rather than of diagnosis for the orthopaedic surgeon. This is evident in the pattern of frequency rates for fractures in motorist casualty survivors (Fig. 34).

Oddly enough, the more comminuted fractures require the more conservative forms of treatment, simply because most operative procedures cannot be applied to these fragmentary bones (Fig. 35). This is especially true of fractures of the femur from knee-dash impacts. Of late this condition seems to have been on the increase. But it goes almost without mention that conservative measures may require even greater versatility (and watchfulness) on the part of the physician or the specialist than opera-

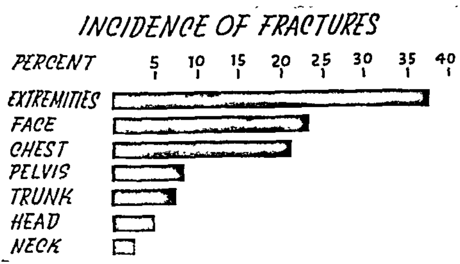


FIG. 34. Frequency rates of fractures observed in a series of more than 650 motorist casualty survivors.

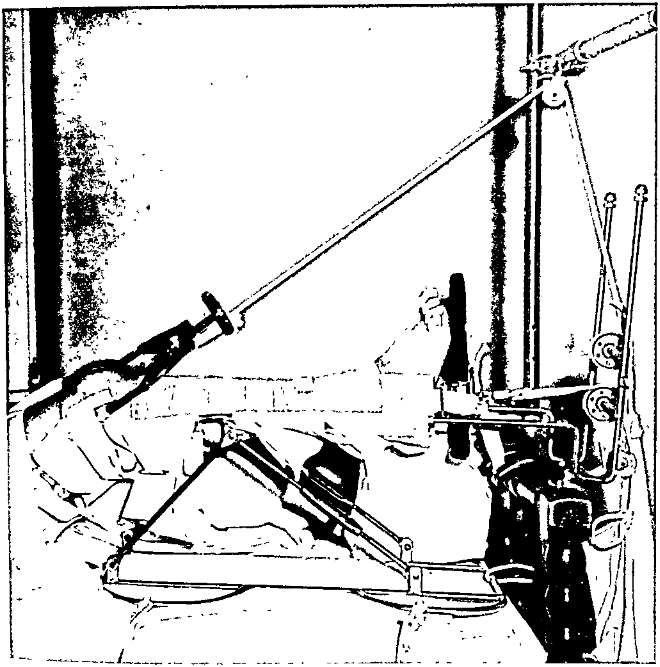


FIG. 35. The more severely comminuted the fracture the more adaptable it is to older and classic methods of skeletal traction. A balanced type of suspension and traction is preferable to that shown above.

tive fixations There must be careful supervision; for example, of the traction devices. And of more importance, one must be on the alert to distinguish between primary injury manifestations and subsequent complications: thromboembolic phenomena, fat embolism, pulmonary congestive and pneumonic states, nephrosis, infections (especially gas bacillus), neurocirculatory disturbances in extremities, and the effects of the treatment itself in regard to rate and quality of healing. Included in the last, of course, is early functional return with prevention of undue atrophy and deformity.

POSTCLINICAL: MEDICOLEGAL

About 50 per cent of patients with residual disabilities of the motorskeletal system require some kind of medicolegal consideration (rehabilitation). A good illustration of this was noted in the author's recent study of 230 persons with so-called "minor" in-



FIG. 36. Early post-traumatic arthritis in the left hip 5 years after bilateral knee-dash impact dislocations, the left one being complicated by a small fracture of the femoral head (closed reductions). The patient was the driver.

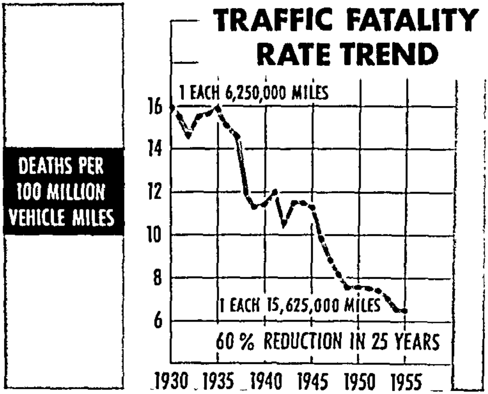
juries of the spine from motor-vehicle accidents. As has been mentioned, this series of neck and lumbar complaints comprised about 65 per cent of the total number of residual disabilities of the motorskeletal system seen by the author from 1947 until July, 1956 (Fig. 36). It was found that isolation, classification and correlation of these cases with the accident configurations that produced the injuries were most helpful for the diagnosis and medicolegal evaluation. This was especially notable with regard to the spinal series. Four chief categories emerged, i.e., sprains, dislocations, herniated disks and fractures. Admittedly, about thr fourths were sprains (with about 10% moi in the lumbar than in the cervical region. However, the relatively large number (grosser skeletal lesions—derived from sim lar accident configuration patterns—serve to temper one's clinical judgment with re gard to medicolegal evaluation and disposi tion when confronted by the patient wit "negative x-ray findings."

All kinds of accident patterns cause these spinal injuries. However, the greate frequency rates of rear-end and angular col lisions must be taken into special account

TABLE 10. ACCIDENT CONFIGURATIONS RELATED TO TYPE OF INJURY IN 230 CASES WITH CERVICAL AND LOW BACK DISABILITIES

ACCIDENT CONFIGURATION (PERCENTAGES)	CERVICAL LESIONS		LUMBAR LESIONS	
	SPRAIN	GROSSER	SPRAIN	GROSSER
Rear-end collision	36.55	31.82	22.02	17.24
Angular collision	22.58	15.90	11.01	13.80
Forward collision	18.28	15.90	25.60	13 80
All others	22.59	36.38	41.37	55.16
	100.00	100.00	100.00	100.00

FIG. 37. Graph supplied by A. L. Haynes, of the Ford Motor Company. (Design Factors in Automotive Safety, SAE summer meeting, June 12-17, 1955.



particularly with respect to cervical lesions (but less so for low back ones). This point is stressed because "whiplashing" has been presumed to be almost exclusively a function of linear types of decelerative and/or accelerative forces. In point of fact almost every type of collision and noncollision accident has been known to produce almost identical clinical patterns in regard to cervical and low back sprains (and grosser skeletal injuries). The frequency of angular collision forces has been noted.

It is to be noted that the more mobile cervical region is quite vulnerable to all kinds of forces and directions of forces (principal impacts), while the more stable lumbar area appears to be chiefly vulnerable to linear types of crash forces. This is reflected in the degrees of injuries received in this series of 230 spinal disabilities (Table 11).

Of the 16 herniated disks, only 1 occurred in the cervical region. The low back dislocations were all in the sacro-iliac joints (subluxations). Most of the fractures were in the posterior and the lateral elements in the cervical vertebrae (first and second as well as third and lower down). The low back fractures affected both vertebral bodies and excessory processes.

TABLE 11. DIAGNOSTIC CLASSIFICATION (275 LESIONS) IN 230 CASES WITH SPINAL INJURIES (PERCENTILE VALUES)

DIAGNOSIS	CERVICAL	LUMBAR	TOTAL
Sprain	67.88	78.98	73.45
Dislocation ..	18.90	2.91	10.91
Herniated disk	0.81	10.78	5.79
Fracture	12.41	7.24	9.85

Certain deductions, based on the apparent relationships that appear to exist between accidents and injuries, are permissible with regard to residual cervical and lumbar complaints. First, there are the injuries that occur in guest passengers. These persons are relaxed (off guard) for the most part. Therefore, it is likely that factors responsible for the intrinsic stability of the spine—ligaments, joints, intervertebral disks—are subjected to excessive stresses in these people. The dynamic functions of the driving functions may serve to modify both force applications and reactions to these forces. Be



FIG. 38. Symbol of controllability of motor-vehicle accidents; historic full-scale automobile crashes studied by Herman Roth, then of the Institute of Transportation and Traffic Engineering, University of California at Los Angeles. (Physical Factors Involved in Head-on Collisions, Highway Research Board Proceedings, Dec., 1951)

that as it may, in this series there were slightly more passengers than drivers. It is to be noted that every seat in the automobile (and other vehicles) has similar injury potentials in regard to this type of injury to the spine.

Sometimes, in spite of the most careful differential diagnostic procedures and examinations, some doubt lingers in the mind of the conscientious clinician with regard to sprains (and even some grosser lesions). Ordinarily this is intensified with respect to medicolegal cases for obvious reasons. In this series, however, the diagnostic assurance was greater in the medicolegal cases than in the private ones, probably because the former usually permit a better differential range of consultations, etc.



FIG. 39 Symbol of preventioneering: plastic methods of suturing facial lacerations *(left)* will prevent severe scarring *(right)*.

The chief pitfalls to be avoided are the accessory (concurrent) physical deficiencies thus brought to clinical attention. Again, in this series, arthritis and related conditions were the critical factors contributing to uncertainty in regard to diagnosis and medicolegal evaluation. It is a striking fact that uncomplicated cases are uncommon in both private and medicolegal cases.

GENERAL COMMENTS

The epidemic number of crash injuries and deaths is tending to advance new horizons of medical participation in reducing accidents and injuries (Fig. 37).

In regard to accident prevention, there is only one clear-cut approach for medicine, i.e., medical screening for driver licensure (and maintenance of driver fitness). Admittedly, the obstacles confronting physicians here are formidable. The first step is not difficult: a positive attitude. Secondly, the reduction of injuries is also largely dependent upon medical screening of a sort, i.e., the accumulation of valid medical data with regard to the physical condition not only of drivers but of the motoring population in general. The high rates of physical disabilities noted in the series of 230 cases with spinal injuries intensify the need for the incorporation of ever larger factors of safety into all ground motor vehicles. To be effective, demands in this direction must be based upon scientific facts (Fig. 38).

Preventioneering has been the physician's credo for many ages (Fig. 39). Yet, for one reason or another, many physicians are loath to accept one of the greatest challenges along these lines ever to confront this country's public and individual safety and health.

So great and widespread a problem can be solved only by the participation of the general public. There seems to be no simpler or surer way to achieve this than through real medical screening. The benefits accruing from this kind of action are well known to industry and the armed forces.

The physician's part has to do chiefly with the human variables involved. It is significant that the bulk of the driver responsibility rests solidly with those between 21 and 45 years of age. The proximal and the distal fringe-age areas also have their share in it, but not the bulk of it (youths and gerontols). The implications regarding the share that industry and the armed forces have in motorist safety should be clear.

With regard to his patient's immediate automotive environment, the doctor should be concerned with automotive design for survival. The fact that all types of motor vehicles are involved in injury-producing accidents indicates that these must all be scrutinized from both the human and the crash-impact engineering standpoints. However, the fact that the vast majority are private automobiles cannot be forgotten. But, since trailers and station wagons are gaining in popularity with private drivers, these two designs or models should receive the bulk of attention from safety engineers in addition to the regular automobiles. The fact that trailers and station wagons have capacities that approach those of commercial carriers is a sobering thought from the standpoint of injury potential.

CONCLUSIONS

The large number of acute and chronic injuries of the motorskeletal system is alerting orthopaedic surgeons (and others) to the *extraclinical* as well as *clinical* and *postclinical* problems that these results of motor-vehicle accidents are producing.

The chief preclinical areas that beg for exploration and development include investigations into connections between physical deficiencies and greater-than-chance accidents and accidental injuries.

Next in importance (chronologically) is the need for improved first aid.

Thirdly, emergency care must be brought up to levels of diagnosis and treatment in keeping with modern advances along these lines This means better admission services

and better medical organization regarding this service.

Fourth, the team approach for the dangerously injured person must be recognized Such cases require, among other attentions, the services of an internist.

The increasing number of medicolegal complications calls for a more equitable attitude toward these problems by all those who accept the responsibility of caring for these *victims in the first place.*

BIBLIOGRAPHY

Accident Facts, 1956 edition, National Safety Council.

Campbell, H.: Role of safety belt in 19 auto crashes, Bull. Am. Coll. Surgeons 40:155, 1955.

Funston, R. V.: Dashboard dislocation of the hip, J. Bone & Joint Surg. 20:124, 1938.

Gay, J. R., *et al.*: Common whiplash inju of the neck, J.A.M.A. 152:1698, 1953.

Kulowski, J.: Orthopaedic Aspects of A mobile Crash Injuries and Deaths (S posium), Annual Meeting, A.M.A., Chic 1956.

Kulowski, J., Long, F. C., Baker, W., and I ley, G.: Automobile crash protrusion femur at knee, Am. Pract. 7:1605, 195

Kulowski, J., and Rost, W. B.: Adhesion terminal ileum to brim of pelvis from sa belt, A.M.A. Arch. Surg., in press.

Orthopaedic Aspects of Motor Vehicle A dents, Annual Meeting, Southern M. Washington, D.C., 1956.

Roth, H.: Physical Factors Involved in H on Collision of Automobiles, Highway search Board Proceedings, Dec., 1951.

Severy, D. M.: Controlled automobile r end collisions, Canad. Services M. J. 11: 1955.

Stapp, J. P.: Criteria for Crash Protectio Armed Forces Ground Vehicles, HA Technical Note, April, 1956.

Index